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The Relationship between Health Literacy, Patient Activation, and Health Outcomes in Breast Cancer Patients

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The Relationship between Health Literacy, Patient Activation, and Health Outcomes in Breast Cancer Patients

by

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Dedication

I dedicate this book to my Almighty Father; He is the source of my strength and my guiding light. I also dedicate this book to my sons, Kene and Kobi who have filled my life with so much joy; my husband, Dr Obiajulu Kanu, who always encourages me to leave my comfort zone and reach for the stars; and my loving parents, Mazi and Dr (Mrs) Chimah who tirelessly support my dreams.

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Abstract

The Relationship between Health Literacy, Patient Activation, and Health Outcomes in Breast Cancer Patients

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The aim of this study was to evaluate the level of health literacy and patient activation in a sample of breast cancer patients as well as examine the relationships of these constructs to health outcomes.

A cross-sectional study design was employed. HER-2 positive breast cancer patients receiving care at 12 oncology clinics in Texas who had scheduled office appointments between August and October 2018 were approached to participate in the study via convenience sampling. Patients who expressed willingness to participate in the study were given a 67-item survey to complete during their office visit. The survey consisted of the 6-item cancer health literacy measure (CHLT-6), the 6-item newest vital sign (NVS), the 13-item patient activation measure (PAM 13), the 27-item functional assessment of cancer therapy (FACT-G v. 4), two items measuring the quality of patient-provider communication, and single item measures for the number of ED visits/hospitalizations as well as clinical and demographic patient characteristics. All variables were analyzed descriptively (means, frequencies). Bivariate and multivariate analyses were also conducted to assess the relationships between variables and predict health outcomes.

Almost 90 percent (N=146) of the 164 patients approached participated in the study. Results from the 146 study participants showed that the average age was 57.1±10.8 years. The majority were female (99%), Caucasian (72%), married or in a relationship (70%), at least had a college degree (53%), and had an annual household income over $50,000 (66%). Clinically, there was an almost equal distribution of patients from cancer stage 1 to stage 4 and most patients had been diagnosed for the first time within the last 5 years (78%). Ninety-two percent (N=134) of participants had adequate cancer health literacy while 79 percent (N= 114) had adequate general health literacy based on their CHLT-6 and NVS scores, respectively. The mean patient activation score was 65.9±15.7 (of a possible 100) with most patients (68%, N= 99) in the higher levels (level 3 or 4) of activation. The average quality of life based on an overall FACT-G score of 108 was high (82.6±16.1). Bivariate analysis showed significant positive relationships between cancer health literacy and educational level, and household income. Ethnic minorities were also found to have significantly lower patient activation scores compared to Whites. Multivariate analysis revealed that cancer health literacy, patient activation, educational level, and number of treatment types received explained 23 percent of the variation in quality of life, and all except cancer health literacy were positive and significant predictors.

It is important to pay attention to modifiable factors such as patient activation that impact breast cancer patients' quality of life in interventions aimed to improve quality of life, especially in ethnic minorities who tend to have lower patient activation levels. The high levels and homogeneity of cancer health literacy among study participants could have influenced its non-significant relationship with quality of life. Further assessments of health literacy and patient activation with quality of life as well as other health outcomes in larger and more diverse populations of breast cancer patients are warranted.

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Chapter 1: Introduction

This chapter gives a brief overview of breast cancer, its economic impact, the current treatment therapies, and the disease outcomes. It also introduces the concept of health literacy and patient activation. Patient activation aims to make patients with chronic diseases partners in their disease management while health literacy embodies the cognitive and social skills that determine the motivation and ability of individuals to use health information. Finally, the study significance discusses the gap that this study aims to fill by assessing the relationship between patient activation, health literacy, and health outcomes in breast cancer patients.

1.1 Breast Cancer

Breast cancer refers to a group of diseases that affect breast tissue typically resulting from an uncontrolled growth of breast cells. Five to ten percent of breast cancers are due to inherited genetic abnormalities while 85 to 90 percent are due to genetic abnormalities resulting from the aging process and lifestyle.[1] The symptoms of breast cancer are generally non-specific. However, the most common symptom is a new lump in the breast or underarm. The classification of breast cancer depends on which breast cell becomes cancerous. Breast cancer can begin in the breast lobules, ducts, or connective tissue. The lobules produce milk, the ducts carry milk from the lobules to the nipple, and the connective tissue provides the breast framework. The majority of breast cancers begin in the ducts or lobules and less commonly in the stromal tissues, which include the fatty and fibrous connective tissues of the breast. The two main manifestations of breast cancer are invasive ductal carcinoma and invasive lobular carcinoma. Other less common kinds of

breast cancer include Paget's disease, medullary, mucinous, and inflammatory breast cancer.[2]

Cancerous breast cells can usually spread over time, invading nearby healthy breast tissue and making their way into the underarm lymph nodes, from where they travel to other parts of the body. Breast cancer staging refers to how far the cancer cells have spread beyond the original tumor site. The spread of cancer at the time of diagnosis determines the staging. Appropriate staging is necessary to determine treatment options and assess disease outcome. Clinicians generally prefer the TNM staging system which assesses cancers based on the tumor size (T), whether it has grown to involve nearby areas, absence or presence of regional lymph node involvement (N), and absence or presence of distant metastases (M). A tumor is assigned to a stage of 0, I, II, III, or IV after the T, N, and M categories are determined. Stage 0 refers to a noninvasive cancer which is limited to the cells of origin while stage IV is the most advanced, fully metastasized stage.[3]

Breast Cancer Epidemiology

Men and women can get breast cancer, but it is much more common in women. In United States women, breast cancer is the second most common cancer. Advanced age, genetic mutations, sedentary lifestyle, and the use of certain oral contraceptives are some factors that influence the occurrence of breast cancer. The risk of breast cancer increases with age, with an average age at breast cancer diagnosis of 61 years among women. About 19 percent of breast cancers occur among women younger than 50 years, and 44 percent occur in women older than 65 years.[2,3] In the United States, about 220,000 cases of breast cancer are diagnosed in women and about 2,000 in men, annually. Approximately 40,000 women and 400 men die every year from breast cancer in the United States. It is the leading cause of cancer death among Hispanic women and the second leading cause of cancer death

among women in general. However, breast cancer deaths have declined over time. Over the last decade, the risk of getting breast cancer has not changed for women overall, but the risk has increased for black, Asian, and Pacific Islander women. Black women generally have a higher risk of death from breast cancer than white women.[2]

Breast Cancer Management

Advances in medicine have changed the prognosis for previously terminal diseases like cancer. In the United States, an appreciable percentage of individuals (41%) diagnosed with breast cancer have survived for a number of years after diagnosis.[4] Improvements in treatment and earlier detection have increased the 5-year relative survival rates for female breast cancer patients in the past three decades with 5-year, 10-year, and 15-year breast cancer relative survival rates of 89 percent, 83 percent, and 78 percent, respectively.[3,5]

The treatment choice for breast cancer depends on the breast cancer type and degree of spread. Surgery, chemotherapy, hormonal therapy, biological therapy, and radiation therapy can be employed to treat breast cancer independently or in combination.[3] Breast cancer treatment usually involves breast-conserving surgery (lumpectomy/partial mastectomy), which involves removal of only cancerous tissue accompanied with radiation or non breast-conserving surgery (mastectomy) which involves surgical removal of the entire breast. With successful breast conserving surgery, long-term survival is the same as in treatment with mastectomy.[6,7] Women under 40 years of age and patients with larger and/or more aggressive tumors are more likely to undergo mastectomy.[8] In addition, patients eligible for breast-conserving surgery might opt for a mastectomy for reasons such as fear of recurrence or a reluctance to undergo radiation therapy.[9,10] Following this description of breast cancer, its epidemiology, and disease management, is an explanation of the health literacy construct which is the primary independent variable in this study.

1.2 Health Literacy

Health literacy refers to an individual's ability to obtain, communicate, process, and understand basic health information and services in order to make appropriate health decisions.[11,12] It is a complex phenomenon which involves individuals, families, communities, and systems. Health literacy incorporates a range of abilities including reading, analyzing information, decoding instructions, weighing risks and benefits, and making healthcare decisions.[13] Individuals are increasingly being held accountable for making healthy lifestyle choices and managing their health in complex health care systems but are ill-prepared to take on these roles.[14] Health literacy may be worse than an individual's general literacy.[15] In the United States, up to 90 million adults have low health literacy which translates into difficulty with understanding and using health information. Risky behaviour, poorer health, less self-management and more hospitalization result from weak health literacy competencies.[13] These negative outcomes place a significant strain on human and financial resources in the health system.[13]

Health Literacy Measurement

Current instruments for measuring health literacy skill levels mainly capture an individual's ability to read. There is no gold-standard instrument to adequately assess the global health literacy concept by capturing the interactions of reading ability, numeracy, and oral literacy. The most commonly used instruments to measure general health literacy are the Rapid Estimate of Adult Literacy in Medicine (REALM) and the Test of Functional Health Literacy in Adults (TOFHLA).[16] Other instruments like the Newest Vital Sign (NVS) are also used to assess general health literacy in clinical practice.[17] However, in 2014, Dumenci et al. developed a cancer-specific health literacy instrument which measures cancer health literacy as a binary construct. Individuals are classified as either

having limited cancer health literacy or adequate cancer health literacy based on their responses to the six items in the instrument. There is evidence that supports the instrument's reliability and validity. It has also been shown to have a high degree of specificity and sensitivity. Compared to individuals with adequate cancer health literacy, individuals with limited cancer health literacy are likely to be Black, under-educated, have low income, not be privately insured, and tend not to engage in health decisions.[18]

Health Literacy and Cancer Care

Cancer care in the United States is sub-optimal and the effects of the poorly coordinated, and fragmented system result in difficulties with coordinating care, accessing care, and obtaining relevant health information by oncology patients.[19] Patients with low health literacy are particularly affected by this complex healthcare system with a limited capacity to obtain, process, and understand both written and verbal cancer information as well as access and navigate the system. This complex of factors significantly contribute to the high cancer mortality rates in the United States.[12,20]

Health literacy is an important element in effective cancer communication, and it is often overlooked.[21] Functional literacy is context-specific and in the case of cancer, it is likely that a significant number of individuals, regardless of literacy levels, lack a clear understanding of cancer control guidelines and screening recommendations. People that have been screened for cancer may lack basic understanding of test results and even cancer patients may lack adequate knowledge of treatment recommendations and clinical trial options.[13]

An explanation of the patient activation construct, which is the secondary independent variable in this study, and is thought to mediate the effect of health literacy on health outcomes, follows.

1.3 Patient Activation

Patient engagement is a broad concept that includes patient activation, the interventions designed to improve patient activation, and patients' behavior as result of such interventions. Patient activation itself, refers to a patient's understanding of his/her role in the healthcare process and the possession of knowledge, confidence, and skills to facilitate active participation in managing their health. This motivates a patient to become engaged by taking preventive actions, collaborating with providers, managing symptoms and problems, and finding and using high-quality and appropriate care.[22-24]

Patient Activation Measurement

Patient activation is a latent construct which can be measured using the patient activation measure (PAM). The PAM is a series of questions that estimate an individual's self-concept as a manager of his or her health and health care with response options that are degrees of agreement or disagreement. It was developed by Hibbard et al. in the early 2000s and is a unidimensional and probabilistic, Guttman-like scale with evidence of validity and reliability. The PAM enables the assessment of an individual's knowledge, skills, beliefs and confidence for managing health and healthcare.[24,25] Activated patients understand that, apart from the care and support of medical practitioners, the sustenance of good health depends on their knowledge of their disease condition, the possession of skills to manage their symptoms and the confidence to take appropriate action when necessary.

Impact of Patient Activation on Health Outcomes

Patient activation is a measurable intermediate outcome of care that is linked with health outcomes.[22] Studies have shown that patients with chronic conditions including diabetes and heart failure who have high activation levels place a lower burden on the health system and have better health outcomes.[25-28]

Patients with low activation are twice as likely to delay medical care, and three times as likely to have unmet medical needs compared to patients with high activation.[29] In addition, highly activated patients get more out of available healthcare services due to their greater involvement in disease management. They are at least two times as likely to prepare questions for a physician visit, to know about treatment options for their disease, to seek health information, and to compare the quality of health care received from providers than patients with low activation.[30,31] Consequently these highly activated patients are less likely to be hospitalized or visit the emergency department.[25,32]

Patient activation is a modifiable factor and interventions tailored to individual patients' activation levels have been shown to be effective in increasing patient activation. However, patients with the lowest activation tend to have greater improvements in activation when interventions are introduced compared to patients who already have high activation levels due to a ceiling effect.[22,32-34] It is important to tailor interventions to a patient's activation level by encouraging realistic behavior modifications. Such strategies have a greater chance of successfully increasing patients' activation levels because challenging behaviors are less likely to be adopted by patients with low activation.[23]

Racial/Ethnic Variations in Patient Activation

Compared to Caucasians and African Americans, Hispanics have much lower levels of patient activation with only 24.8 percent of Hispanics at the highest level of patient activation (activation level 4), compared to 39.5 percent of blacks and 45.3 percent of whites. Low acculturation and ability to navigate the American healthcare system have been identified as contributory factors to these differences which persist even after controlling for other demographic and socioeconomic factors. In addition, Hispanic breast cancer patients have the greatest odds for decision dissatisfaction and are more vulnerable to poor breast cancer treatment decision outcomes than patients of other ethnicities. Consequently, increased patient activation among this patient population might significantly reduce disparities in their access to and use healthcare.[35,36]

Patient Activation and Health Promoting Behaviors

Irrespective of disease type and economic level, highly activated patients have greater adherence to treatment regimens and are more likely to regularly perform self-monitoring as well as obtain regular chronic care.[25,31,37-39] A number of studies have examined the impact of activating patients with different chronic diseases such as diabetes, depression, HIV and hypertension and the results of these studies show the financial, clinical, and psychological benefits of such interventions.[40-42] In addition, a recent study by O'Malley et al. specifically investigated the determinants of patient activation in a predominantly Caucasian (77%) and African American (15%) cohort of breast and prostate cancer survivors. The study results revealed that among the 213 breast cancer survivors, overall patient activation was high with a mean of 3.34±0.37 and this was significantly higher than that of the 112 prostate cancer survivors (3.25±0.38). Race, marital status, employment status, household income, and fear of recurrence were significantly associated

with patient activation for only prostate cancer survivors. Non-Caucasian, unmarried, unemployed, and low-income prostate cancer survivors had lower activation scores than Caucasian, married, employed, and high earning survivors, respectively. However, for both breast and prostate cancer survivors, ease of access to and perceptions of time spent with healthcare providers (oncology team and primary care physicians) were positive predictors of activation.[43]

1.4 Study Significance

Patient activation and health literacy are independent predictors of health and deficits in either of them could serve as targets for behavioral intervention.[44,45] Higher activation helps individuals with low literacy and numeracy abilities to compensate for their lower skills and to achieve higher levels of comprehension. When health trade-offs are necessary, making the right choice depends on literacy and comprehension as well as patient activation.[46]

A study by Hibbard et al. investigating the relationship between patient activation and health literacy showed that among older adults, both health literacy and patient activation were significantly and positively related to healthcare decision making, even though this relationship was stronger for health literacy.[47] Patient activation had slightly stronger relationships to health-care-related behaviors, healthy behaviors, and self-management behaviors than health literacy.[47] Another study by Nijman et al. which examined the relative contribution of patient activation and functional health literacy to the seeking and use of health information showed that more activated consumers were more likely to seek and use health information. In the study population, health literacy increased as patient activation increased, with a weak to moderate overall correlation between the health literacy and activation scores.[48]

Recent studies in oncology reveal that health literacy and certain aspects of patient activation are associated. A cross-sectional, multicenter oncology study that examined patient activation, health literacy, symptom burden, confidence to self-manage side effects, and medication adherence to oral oncolytics showed that confidence to self-manage side effects (e.g., fatigue and diarrhea) were associated with higher health literacy and higher patient activation.[49] Another study revealed that higher patient activation increases colorectal cancer screening in low income, minority patients with limited health literacy skills.[50]

However, these studies were conducted in homogenous patient populations (95% Caucasian), were not specific to breast cancer patients, or did not illustrate the relationships of patient activation and health literacy to health outcomes and resource utilization. Measuring patient activation and health literacy will facilitate the provision of activation stage-appropriate information to breast cancer patients at their literacy level and thereby can increase the effectiveness of interventions geared toward improving patient involvement in managing their health.

Chapter 2: Literature Review

This chapter contains the literature review of the major concepts in this project. The first section gives a detailed description of breast cancer, including its epidemiology, pathogenesis, diagnosis, treatment options, and economic burden. The second section discusses health literacy in the oncology space with emphasis on breast cancer patients. The third section reviews patient activation in chronic disease management with particular emphasis on its relevance in breast cancer patients. The final two sections explain the theoretical framework that this study is based on as well as the study significance.

2.1 Breast Cancer

Breast cancer refers to a group of diseases caused by the formation of malignant cells in breast tissues. These malignant cells are characterized by uncontrolled division resulting in abnormal growth. If left untreated, malignant breast cells can invade surrounding tissue, spreading to other parts of the body through blood and lymph vessels and leading to metastasis.[2,51]

2.1.1 Breast Cancer Epidemiology

Breast cancer is the most common cancer in women globally with about 1.7 million new cases diagnosed in 2012.[52] There are generally higher rates of breast cancer in developed countries compared to developing countries. These differences might be due to lifestyle and reproductive patterns prevalent in developed countries. In addition, poor screening rates and incomplete reporting practices in developing countries play a role in fostering this disparity. Even though breast cancer is presumed to be a disease of the

developed world, about 69 percent of all breast cancer deaths occur in developing countries.[52-54]

Breast cancer incidence rates vary greatly worldwide, with North America having the highest rate of up to 99.4 per 100,000. Eastern Europe, South America, Southern Africa, and Western Asia have moderate incidence rates, while African countries have the lowest incidence rates. The incidence rates are steadily increasing in moderate and low incidence areas. The pattern of cancer incidence in developing countries is expected to increasingly mirror that of developed countries with increasing westernization.[52,55]

Although breast cancer occurs in males and females, it is much more common in women. In the United States, the American Cancer Society estimated 252,710 and 2,470 new cases of invasive female and male breast cancer in 2017, respectively. In addition, 41,070 female and 460 male breast cancer deaths were estimated in 2017.[56] Breast cancer is the second most common cancer representing 14 percent of all new cancer cases in the United States and is the second leading cause of cancer death among women in general. The average American woman has a 12 percent risk of developing breast cancer in her lifetime.[55,57]

Breast cancer incidence and death rates differ by ethnicity and geography in the United States. Generally, non-Hispanic White and Black women have higher rates than women of other racial or ethnic groups. Asian and Pacific Islander (API) women have the lowest incidence and death rates. Furthermore, White women have appreciably higher breast cancer incident rates than Black women between the ages of 60 and 84, while Black women have higher incidence rates before age 45 and are more likely to die from breast cancer at every age.[55] A combination of factors are responsible for the higher mortality rates in Black women including later stage at diagnosis, obesity, comorbidities, and tumor characteristics. Poor access, adherence, and response to treatment as well as sub-optimal

mammography screening also contribute to this disparity.[58-61] In 2012, breast cancer death rates were 42 percent higher in Black than White women.[55]

In general, breast cancer deaths have declined over time and the risk of getting breast cancer has remained constant for women overall. However, over the last decade, the risk of getting breast cancer has increased for Black, and API women.[2] Generally, breast cancer death rates per 100,000 women are higher for Black women than non-Hispanic White women. Breast cancer death rates range from 18.7 to 25.4 for White women, 21.7 to 35.0 for Black women, 7.8 to 18.3 for Hispanic women, and 7.5 to 16.9 for API women. Breast cancer mortality rates among White women tend to be highest in the North Central, Mid-Atlantic, and Western regions of the United States, while the highest death rates for Black women are in California and some of the South Central and Mid-Atlantic states.[55]

2.1.2 Economic Burden of Breast Cancer

Breast cancer is expensive to treat from both personal and social perspectives. It is responsible for the largest share of cancer-related spending in the United States, constituting 13 percent of all cancer-related spending in 2010. In general, breast cancer diagnosed at an early stage is less expensive to treat than advanced stage breast cancer with an average treatment cost of $71,909, $97,066, $159,442, and $182,655 for stages 0, I/II, III, and IV, respectively in the first 24 months after diagnosis. In the United States, direct breast cancer medical expenses were $16.5 billion in 2010 and these costs are expected to increase to $20.5 billion by 2020.[62,63] Indirect breast cancer medical costs are also significant and mainly result from lost wages, cancer-related death, and out-of-pocket payments for health services including hospitalization and physician visit copayments. Out-of-pocket expenditures and lost income average $1,455 per month and vary widely depending on insurance.[64] Total annual indirect productivity costs for female breast cancer

patients range from $344 million (18 to 44 years) to $1,511 million (45 to 64 years) due to a higher prevalence of breast cancer in the older population (0.3% vs 3%).[65] On average, the financial burden of breast cancer accounts for 98 percent, 41 percent, and 26 percent of monthly income among female breast cancer patients with annual household income levels of ≤$30,000, $30,001-$60,000, and >$60,000, respectively.[64]

Approximately 23 percent of breast cancer expenditures are made during evaluation and management in the year after diagnosis, while 41 percent and 36 percent are spent on continuing care and in the last year of life, respectively. Breast cancer patients usually survive for long periods of time and this explains why the continuing care phase accounts for the largest share of lifetime costs. Breast cancer has the highest continuing care and end-of-life expenditures in comparison to other malignancies.[66] The distribution of costs in the year after diagnosis by type of therapy is about 25 percent, 15 percent, 11 percent, 18 percent and 31 percent for surgery, chemotherapy, radiation therapy, other hospitalizations, and other services, respectively.[67]

Even though total costs have been shown to be greatest during the continuing phase of breast cancer care, the cost per unit of time are greatest during the initial and terminal phases of care. The average annual net costs for women less than 65 years is $27,700, $2,200, and $94,300 per year during the initial, continuing phase, and last year of life, respectively. However, costs are usually lower for women 65 years and older, especially during the last year of life ($62,900 per year).[62]

The out-of-pocket costs for breast cancer patients and their caregivers are approximately $2,700 to $7,900, respectively.[68] For patients who were employed before their diagnosis of breast cancer, lost wages from time spent on treatment and disability have been estimated at $4,300 and $5,900, respectively.[64,69-71] Total lost-productivity costs

from breast cancer deaths were estimated to be $10.9 billion in 2010, accounting for eight percent of all cancer-related productivity losses nationally.[72]

2.1.3 Breast Cancer Risk Factors

The exact cause of breast cancer is unknown. However, engaging in regular physical activity, maintaining a healthy body weight, and breastfeeding for at least one year have been associated with a reduced risk of breast cancer. On the other hand, several factors, both modifiable and non-modifiable, increase the risk of breast cancer occurrence. Potentially modifiable risk factors include excessive weight gain, physical inactivity, postmenopausal hormone use, alcohol consumption, long term smoking, and consistent sleep pattern disruption.[56] Advanced age is a significant non-modifiable breast cancer risk factor, with an average age at breast cancer diagnosis of 61 years in women. About 19 percent of breast cancers occur among women younger than 50 years, and 44 percent occur in women older than 65 years.[2,3] Personal or family history of breast cancer also significantly affects the occurrence of breast cancer. Individuals with a family history of breast cancer, especially in a first-degree relative, have a higher risk of developing breast cancer. This risk multiplies as the number of affected first-degree relatives increases.[73] Inherited cases of breast cancer are usually associated with two abnormal genes: BRCA1 (BReast CAncer gene 1) or BRCA2 (BReast CAncer gene 2). Abnormal *BRCA1* or *BRCA2* genes are found in five to 10 percent of all breast cancer cases in the United States. Women who inherit a mutation in either of these genes have about a 60 percent risk of being diagnosed with breast cancer during their lifetimes which is much higher than the 12 to 13 percent risk for women overall.[74,75]

Other non-modifiable risk factors include high breast tissue density, high-dose radiation to the chest at a young age, and type 2 diabetes. In addition, recent use of oral

contraceptives, never having children, having one's first child after age 30, long menstrual history, and high level of sex hormones are reproductive factors that increase breast cancer risk.[56]

2.1.4 Breast Cancer Signs and Symptoms

The symptoms of breast cancer are generally non-specific. There are usually no symptoms when the breast tumor is small and has the best likelihood of positive treatment response. However, the most common sign is a new lump in the breast or underarm. Breast cancer can spread to underarm lymph nodes causing a lump or swelling before the breast tumor itself can be felt. Besides cancer, many other conditions can cause breast lumps including breast fibrosis and simple cysts, adenosis, fibroadenomas, and phyllodes tumors. In general, persistent changes in the breast should be evaluated by a physician as soon as possible. Pain is not a good indicator of breast cancer occurrence. In addition to breast lumps, other signs of breast cancer include:[2,55]

- Thickening or swelling of part of the breast.
- Irritation or dimpling of breast skin.
- Redness or flaky skin in the nipple area or the breast.
- Pulling in of the nipple or pain in the nipple area.
- Nipple discharge other than breast milk, including blood.
- Any change in the size or the shape of the breast.
- Pain in any area of the breast.

2.1.5 Detection of Breast Cancer

Breast cancer screening involves checking for breast cancer prior to the manifestation of any signs or symptoms. Breast cancer screening does not prevent breast cancer. However, early detection is associated with a greater number of treatment options and an increased likelihood of treatment success.[76] The two main tests used for breast cancer screening are mammograms which produce an X-ray of the breast, and breast magnetic resonance imaging (MRI) which uses magnets and radio waves to produce an image of the breast. Breast MRIs are used along with mammograms to screen women who have a high risk for getting breast cancer. They are not used for women at average risk because MRIs may appear abnormal even when there is no cancer. Breast ultrasound and biopsies are additional techniques that are used to diagnose breast cancer. The United States Preventive Services Task Force (USPSTF) recommends that 50 to 74-year-old women with an average risk for breast cancer should get a mammogram biannually. Current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older. Women younger than 50 years are advised to weigh the benefits and risks of screening tests with the guidance of their healthcare provider when making decisions about when and how often to get mammograms.[2,77]

2.1.6 Breast Cancer Classification

Even though breast cancer is generally considered to be a single disease, it is actually distinguished by different subtypes which vary in biological presentation, treatment response, and outcomes. In addition, these subtypes are associated with distinct risk factors. Breast cancer can be classified based on histopathology, molecular characteristics, and cancer stage.[55] Details of these subtypes are described below.

A. Classification Based on Histopathology

The classification of breast cancer based on cancer type depends on which breast cell(s) becomes cancerous. Breast cancer can begin in the breast lobules, ducts, or connective tissue. The lobules produce milk, the ducts carry milk from the lobules to the nipple, and the connective tissue provides the breast framework. The majority of breast cancers begin in the ducts or lobules and these cancerous cells could either be confined to the cells where they originate (*in situ*) or spread to other areas of the body (invasive). The few cancers that start in other breast tissues are considered to be sarcomas and lymphomas. Other less common kinds of breast cancer include Paget's disease, medullary, mucinous, and inflammatory breast cancer.[2,55,57] Details of the different breast cancer types are discussed below.

1. Breast Cancer *in situ*

Intraductal carcinoma

This type of breast cancer is also referred to as ductal carcinoma *in situ* (DCIS) and makes up about 20 percent of new breast cancer cases. It occurs when the normal epithelial cells of the breast ducts are replaced by abnormal cells, leading to considerable expansion of the ducts and lobules. The abnormal cells in this noninvasive form of breast cancer do not grow beyond the cells of origin. DCIS may or may not progress to invasive cancer over time but, because it is impossible to predict the disease progression, almost all women with a diagnosis of DCIS receive treatment.[55,57]

Between 2008 and 2012, 83 percent of newly diagnosed *in situ* female breast cancer cases were DCIS. There are about 60,000 DCIS cases diagnosed in the United States annually. Individuals who had a prior episode of DCIS have a higher risk for recurrence and development of a new breast cancer than those who have never had breast cancer. The

chances of a recurrence are under 30 percent and recurrences usually occur within five to ten years of the initial diagnosis[55,75]

Intralobular Carcinoma

This type of breast change is also referred to as lobular carcinoma in situ (LCIS) or lobular neoplasia and consists of cancer-like cells growing within the breast lobules. Even though the name includes the term "carcinoma," LCIS is not a true breast cancer. It is not generally considered to be a precursor of invasive cancer because it does not spread if left untreated. However, it is thought to indicate an increased risk of developing invasive cancer. LCIS does not typically have conspicuous symptoms and is typically discovered during a biopsy for another proximal breast problem. LCIS is extremely uncommon in men and is usually diagnosed between the ages of 40 and 50 in women, before menopause. It is less common than DCIS and accounted for about 13 percent of in situ breast cancers diagnosed in women between 2008 and 2012.[55,57,75]

2. Invasive Breast Cancer

Invasive Intraductal Cancer

This type of breast cancer, also known as infiltrating ductal carcinomas (IDC), is the most common type of breast cancer, comprising up to 80 percent of all invasive breast cancers. It typically originates in the breast milk ducts then breaks through the ductal wall to grow into nearby tissues. From this point, it can spread (metastasize) to other parts of the body through the blood and lymph circulatory systems. IDC can affect women at any age. However, it is more common in older women and about two-thirds of women are 55 or older when they are diagnosed.[57,75] Rare subtypes of invasive ductal carcinoma include medullary, tubular, mucinous, papillary, and cribiform carcinomas of the breast.[75]

Invasive Lobular Carcinoma

Invasive lobular carcinoma (ILC), also referred to as infiltrating lobular carcinoma, is the second most common type of breast cancer after invasive ductal carcinoma. ILC typically starts in the milk-producing glands (lobules) and like IDC, it can spread (metastasize) to other parts of the body. ILCs constitute about 10 percent of the 180,000 invasive breast cancers diagnosed in the United States annually. Compared to IDC, ILC may be harder to detect on physical exam and imaging procedures such as mammograms. Consequently, a combination of tests is usually employed in diagnosing ILC. Furthermore, ILC tends to affect more than one area of the breast (multifocal) and in comparison to other types of invasive breast cancer, is more likely to affect both breasts (bilateral).[57,75]

3. Other Breast Cancer Types

Inflammatory Breast Cancer

Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer that constitutes about one percent of all breast cancer cases in the United States. IBC usually starts with a feeling of thickness or heaviness in the breast which results from cancer cells clogging the lymph vessels. IBC is characterized by breast reddening and swelling instead of a distinct lump like in other breast cancer manifestations. It typically spreads quickly, and symptoms can worsen within hours. IBC affects men as well as women. In the United States, IBC is more common in African American women and is typically diagnosed at an average age of 52 years in black women and 57 years in white women. IBC symptoms are similar to mastitis and cellulitis but unlike these bacterial infections, its symptoms are usually confined to the breast and it is not resolved by antibiotic treatment.[75]

Paget's Disease of The Nipple

Paget's disease is also a rare form of breast cancer that constitutes less than five percent of all breast cancer cases in the United States. This cancer usually affects the ducts of the nipple first before spreading to the nipple surface and areola. Unusual changes in the nipple and areola are typically early signs of breast cancer. Most people with Paget's disease (> 97%) also have DCIS or invasive cancer somewhere else in the breast. Paget's disease of the nipple affects men and women but is more common in women and usually develops after the age of 50. The average age at diagnosis is 62 years in women and 69 years in men.[75]

Phyllodes Tumors of The Breast

Also known as phylloides tumor and cystosarcoma phyllodes, these tumors account for less than one percent of all breast cancers. Benign, malignant, and borderline phyllodes grow quickly but are typically contained within the breast. Surgery is required to reduce the risk of local recurrence. Even though phyllodes tumors usually develop when a woman is in her 40s, they can occur at any age. Phyllodes tumors are extremely rare in men.[75]

B. Classification Based on Molecular Characteristics

The genes that a cancer expresses determine the molecular subtype. Routinely evaluated biological markers have been used to identify molecular subtypes of breast cancer. These markers include the presence or absence of hormone (estrogen or progesterone) receptors (HR+/HR-), excess levels of human epidermal growth factor receptor 2 (HER2+/HER2), and a growth-promoting protein (Ki-67) .[55] The main molecular subtypes of breast cancer in order of increasing severity are luminal A breast

cancer, luminal B breast cancer, triple-negative breast cancer, and HER2-enriched breast cancer. These subtypes are described below:

Luminal A Breast Cancer (HR+/HER2-)

This type of breast cancer is estrogen-receptor and/or progesterone-receptor positive, HER2 negative, and has low levels of the protein (Ki-67) which controls the rate of cancer cell growth. Seventy four percent of breast cancers have these characteristics. In general, luminal A cancers are low-grade, tend to grow slowly, are less aggressive than other subtypes, and have the best short-term prognosis.[78,79]

Luminal B Breast Cancer (HR+/HER2+)

This type of breast cancer is similar to luminal A breast cancer being hormone-receptor positive (estrogen-receptor and/or progesterone-receptor positive). However, it could be either HER2 positive or HER2 negative and has high levels of Ki-67. Luminal B cancers account for about 10 percent of breast cancers. They grow a bit faster than luminal A cancers and have a slightly poorer prognosis.[80]

Triple-Negative Breast Cancer (HR-/HER2-)

This type of breast cancer is hormone-receptor negative (estrogen-receptor and progesterone-receptor negative) and HER2 negative. About 12 percent of breast cancers are triple negative. This breast cancer subtype is more common in premenopausal women and those with a BRCA1 gene mutation. In addition, African American women are nearly two times more likely to have this cancer subtype compared to Caucasian women.[81] Triple negative breast cancers have the poorest short-term prognosis compared with other breast cancer subtypes, and this is due, in part, to the lack of targeted therapies for these tumors.[79]

HER2-Enriched Breast Cancer (HR-/HER2+)

This type of breast cancer is hormone-receptor negative and HER2 positive. About 4 percent of breast cancers produce excess HER2 and do not express hormone receptors. Even though HER2-enriched cancers grow faster than other breast cancers and have a poorer short-term prognosis, they can be successfully treated with targeted therapies aimed at the HER2 protein.[55,79]

C. Classification Based on Stage

The spread of cancer at the time of diagnosis and tumor characteristics determine staging. Appropriate staging is necessary to determine treatment options and assess disease outcome. The two common staging systems, the TNM system and the Summary stage system, are described in detail below.

TNM Staging System

This staging system was developed by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC). It is commonly used by medical professionals to stage breast cancer as well as other cancer types. This staging system is based on the extent of the tumor (T), the extent of spread to the lymph nodes (N), and the presence of metastasis (M).[82]

The T category describing the primary tumor is used to denote when the primary tumor cannot be evaluated (TX), when there's no evidence of primary tumor (T0), when there is carcinoma in situ (Tis), and size/extent of the primary tumor (T1 – T4; higher numbers depict greater size). The N category is used to describe when regional lymph nodes cannot be evaluated (NX), when no cancer is found in the lymph nodes (N0), and when there is regional lymph node involvement (N1 – N3; higher numbers depict greater

involvement). Lastly, the M category indicates whether or not there is distant metastases using M0 (no distant metastasis), and M1 (for distant metastasis).[82]

Once the T, N, and M classifications are determined, they are combined to derive an overall cancer stage of 0, I, II, III, or IV. Stage 0 refers to a noninvasive cancer which is limited to the cells of origin while stage IV is the most advanced, fully metastasized stage. Lower stage cancers with minimal advancement typically have a better prognosis, while higher stage cancers are often more advanced but can still be treated successfully with recent advances in oncology medicine.[82]

Summary Stage System

Population-based cancer registries utilize the Surveillance, Epidemiology, and End Results Program (SEER) summary stage system which classifies cancers as in situ, local, regional, or distant by assigning one of nine single-digit codes to describe the tumor extent at the time of diagnosis. The codes for summary staging are in ascending order with higher numbers indicating more advanced tumor growth. The nine possible codes for summary stage are as follows:[83]

0 = In-Situ

1 = Local

2 = Regional disease by direct extension only

3 = Regional disease with only regional lymph nodes involved

4 = Regional disease by both direct extension and regional lymph node(s)

5 = Regional disease that is not otherwise specified

7 = Distant sites or distant lymph node involvement

8 = Benign and borderline CNS tumors

9 = Unknown if there is extension or metastatic disease (unstaged, death certificate only cases)

The TNM and summary staging systems correspond to each other as follows:[55]

- Stage 0 corresponds to in situ stage
- Stage I corresponds to local stage
- Stage II corresponds to either local or regional stage depending on lymph node involvement
- Stage III corresponds to regional stage
- Stage IV corresponds to distant stage

2.1.7 Breast Cancer Treatment

A multidisciplinary cancer care team consisting of medical, surgical and radiation specialists typically collaborate to plan and provide care to breast cancer patients. The treatment choice for breast cancer depends on the breast cancer type and degree of spread. One or more of the following approaches can be employed to treat breast cancer:

- Surgery which involves excision of cancer tissue.
- Chemotherapy which involves the use of medications to shrink or kill the cancer cells.
- Hormonal therapy which involves antagonism of the hormones that cancer cells need to grow.
- Biological therapy which boosts the body's immune system and enables it to fight cancer cells or to control side effects from other cancer treatments.
- Radiation therapy which utilizes high-energy rays (similar to X-rays) to kill the cancer cells.

Breast cancer treatment usually consists of breast-conserving surgery (lumpectomy/partial mastectomy), which involves removal of only cancerous tissue accompanied with radiation or non breast-conserving (mastectomy) which involves surgical removal of the entire breast. With successful breast conserving surgery, long-term survival is the same as in treatment with mastectomy.[6,7] Women under 40 years of age and patients with larger and/or more aggressive tumors are more likely to undergo mastectomy.[8] In addition, patients eligible for breast-conserving surgery might opt for a mastectomy for reasons such as fear of recurrence or a reluctance to undergo radiation therapy.[9,10]

About 61 percent of women with early stage (I or II) breast cancer opt for breast-conserving surgery while 36 percent prefer to have a mastectomy. The reverse case occurs among women with stage III disease, 21 percent of whom undergo breast-conserving surgery while 72 percent opt for a mastectomy. Of women with stage IV breast cancer, 48 percent receive radiation and/or chemotherapy without surgery, 25 percent receive surgery alone or in combination with other treatments, and 28 percent of patients receive no treatment.[3]

Post-surgery, breast reconstruction with either a saline or silicone implant or tissue-based reconstruction (such as flaps) are available for women who undergo mastectomy. Up to 57 percent of women with early stage I or II breast cancer who receive mastectomies undergo reconstructive procedures.[3,10,75]

Systemic therapy is also employed in the management of breast cancer. The choice of chemotherapy, hormonal therapy, or targeted therapy depends on factors like tumor size, number of lymph nodes involved, presence of estrogen or progesterone hormone receptors on cancer cells, and amount of HER2 protein made by the cancer cells.[3] About 84 percent of all female breast cancers test positive for hormone receptors[84] which make these cancers

eligible for treatment with hormonal therapy.[3] Table 2.1 contains a summary of treatment recommendations according to breast cancer sub-type.[85]

Table 2.1: Systemic Treatment Recommendations According to Molecular Sub-Type for Non-Metastatic Disease

Subtype	Type of therapy
Luminal A	Endocrine therapy alone according to menopausal status. Chemotherapy also used in some cases.
Luminal B	Endocrine therapy appropriate according to menopausal status plus adjuvant chemotherapy in some cases
Hormone receptor positive and HER2 positive	Chemotherapy plus trastuzumab plus endocrine therapy appropriate for menopausal status
Hormone receptor negative and HER2 positive	Chemotherapy plus trastuzumab
Triple negative	Chemotherapy (anthracyclines and taxanes most commonly used)

When necessary, hormonal therapy is started upon completion of chemotherapy and radiation. The main drugs employed are tamoxifen and aromatase inhibitors and the choice of hormonal therapy usually depends on a woman's menopausal stage. Tamoxifen is the standard hormonal treatment for premenopausal women and is used for a minimum of 5 years, while tamoxifen and/or an aromatase inhibitor are used in post-menopausal women for 5 to 10 years.[86] Targeted therapies are available for optimal treatment of breast cancers that have certain markers like HER2 which is expressed in about 14 percent of breast cancers. Targeted therapies can be given as single agents or in combination with chemotherapy or hormonal therapy.[3,84]

Despite the efficacy of current breast cancer treatment regimens, breast cancer patients are usually burdened with the unpleasant side effects of treatment.[75] An

individual's health literacy and ability to self-manage health (patient activation) are important factors that influence whether a patient knows if and when to seek care for symptoms instead of unnecessarily enduring a poor quality of life -before worsening symptoms become severe enough to warrant a visit to the emergency department or hospitalization. These factors also influence a patient's ability to coordinate their care. Furthermore, health literacy and patient activation might influence a breast cancer patient's ability to detect new symptoms which could signal a disease recurrence.[11,25,26,47] Early detection of breast cancer recurrence could facilitate treatment at an early disease stage which significantly increases the chances of treatment success and survival,[75] highlighting the potential importance of health literacy and patient activation on health outcomes.

2.2 Health Literacy

Health literacy influences the extent to which a patient engages in self-care and chronic disease management. It is defined as the degree to which an individual can obtain, communicate, process, and understand basic health information and services needed to make appropriate health decisions.[87] Health literacy involves a complex set of skills including reading, listening, speaking, writing, analytical, and decision-making skills which influence an individual's ability to navigate health situations. Health literacy is considered an intermediate health outcome that is influenced by social and cultural factors at home, at work, and in the community as well as educational, communication, and health services factors.[88,89]

Health consumers are increasingly encouraged to become involved in managing their health and healthcare with the paradigm shift towards patient-centered care. This requires individuals to assume new roles in seeking health-related information, understanding rights and responsibilities, and making health decisions for themselves and

others. However, the average patient does not have the necessary skills and knowledge needed to successfully perform these new patient roles.[88] People of all ages, races, income, and education levels are affected by the scourge of limited health literacy, and even highly educated individuals often find typical health information and services to be unfamiliar, complicated, and technical.[90]

The nationally representative health literacy survey (National Assessment of Adult Literacy) conducted by the U.S. Department of Education in 2003 included over 19,000 adults aged 16 and above and classified health literacy into four levels; proficient, intermediate, basic, and below basic. The majority of adults (53%) had intermediate health literacy skills. However, 36 percent of survey respondents had the two lowest health literacy levels, implying that almost 80 million adults in the United States have limited health literacy. These adults would probably have difficulty with even simple tasks such as reading and understanding the instructions on a prescription bottle or filling out an insurance form.[90]

The survey results also revealed that only 12 percent of English-speaking adults in the United States have proficient health literacy skills, with lower socioeconomic and minority groups having the highest rates of limited health literacy. The proportion of adults with below basic health literacy (the lowest level) was lowest for Whites (9%) compared to Blacks (24%), Asian (13%), Hispanic (41%), and American Indians/Alaska Natives (25%). This disparity might be due to the quality of education received by disadvantaged members of these ethnic minority groups as well as language and acculturation barriers.[90]

In addition, almost half (49%) of adults with less than a high school degree had the lowest health literacy level and this percentage decreased significantly as education level increased, with only three percent of college graduates having below basic health literacy. Furthermore, age had a minimal relationship to health literacy among adults who were

under 65 years of age. However, adults who were 65 years or older were more likely to have below basic or basic health literacy skills compared to those under 65. Lastly, over 50 percent of publicly insured and uninsured adults had low health literacy skills compared to less than 25 percent of privately insured adults.[90]

Low health literacy is a major source of economic inefficiency in the American health care system. In 2007, Vernon et al. estimated the cost of low health literacy to range from $106 billion to $238 billion annually, which represents seven to seventeen percent of all personal health care expenditures.[91] In addition, emergency room costs are significantly higher for individuals with inadequate health literacy compared to those with adequate health literacy.[92]

Improving health communication reduces health care costs and increases the quality of health care. Both health care providers and patients play important roles in health literacy and clear communication is essential between these two parties. To achieve a more active role in health-related decisions, patients need to develop strong health information skills while healthcare providers need to utilize effective health communication skills. Furthermore, plain language should be employed in writing printed and web-based information.[1] Such measures will make patients more successful in:

- Finding needed health information and services;
- Communicating their needs and preferences and responding to information and services;
- Processing the meaning and usefulness of the information and services;
- Understanding the choices, consequences and context of the information and services; and
- Deciding which information and services match their needs and preferences so they can act. [93]

2.2.1 Health Literacy and Health Outcomes

Low health literacy can have a significant impact on an individual's health. Individuals with low health literacy have a decreased ability to share in decision-making pertaining to their care.[94] Compared to adequate literacy, low or inadequate literacy has a much stronger correlation to poor knowledge and comprehension of health care services and health outcomes. Low health literacy has also been associated with increased chances of hospitalization, higher prevalence and severity for some chronic diseases, poorer global measures of health, and lower utilization of screening and preventive services.[95] Health literacy has also been associated with preventable emergency department visits. Patients with limited literacy have 2.3 times the number of preventable ED visits resulting in hospital admission compared to individuals with adequate health literacy.[96]

However, the bivariate associations between health literacy and health outcomes often become weak and statistically nonsignificant after adjustments are made for covariates such as age, education, socioeconomic status, health care access, or experience in the health care setting. This raises doubts about whether low health literacy is truly an independent problem or simply a marker of other social problems. Based on these findings, some of the recommendations of Dewalt et al. in their 2004 review article were that future research examining the relationship between health literacy and health outcomes should closely examine factors that could confound (e.g., age, income, and health insurance status) and mediate (e.g., self-efficacy, self-care, trust, and satisfaction) the relationship.[95]

Interventions to increase health literacy and self-efficacy have shown improvements in hemoglobin A1c, glucose, and total cholesterol as well as medication adherence in diabetic and HIV patients.[97-101]

2.2.2 Health Literacy in Cancer Patients

Health literacy is increasingly recognized as a critical factor affecting communication across the continuum of cancer care. Low health literacy has been associated with diminished cancer screening, advanced stage at diagnosis, and reduced quality of patient-physician interaction.[13]

Cancer Screening and Health Literacy

With regards to cancer screening, individuals with low literacy have a limited knowledge of anatomy and cancer-related medical terms. Consequently, they are less likely to comprehend the information contained in cancer control interventions or the medical terms commonly used in patient-physician communication.[13,102]

Individuals' attitudes toward cancer screening and their sources of cancer information are affected by their health literacy level. A study by Davis et al. examined the relationship between reading ability and the knowledge and attitudes of low-income women regarding screening mammography in a convenience sample of over 400 women. Study results showed that compared to women with marginal and adequate literacy, patients with low literacy were significantly more likely to have negative attitudes toward mammograms, considering them to be embarrassing, harmful, painful, or bothersome to get. In addition, these women were more likely to be influenced by friends and relatives in their decision to get a mammogram.[102] In general, limited health literacy has a varied effect on cancer screening compliance. Poor health literacy is associated with less knowledge and more misunderstanding about cancer susceptibility, detection, and prognosis which may influence cancer screening practices.[13]

Cancer Stage at Diagnosis and Health Literacy

Health literacy has also been associated with cancer stage at diagnosis. Bennett et al. conducted a study to evaluate the association between poor health literacy and higher rates of advanced prostate cancer stage at presentation among low-income men receiving care in equal-access medical systems. The study results showed that patients with low literacy skills were more likely to be diagnosed at a later prostate cancer stage. Specifically, men reading below a sixth-grade level were 69 percent more likely to be diagnosed with the most advanced stage (stage D) of prostate cancer than those reading above a sixth-grade level. Compared to white men, black men were almost twice as likely to present with stage D prostate cancer and were significantly more likely to have literacy levels less than sixth grade. However, race was not a significant predictor of advanced-stage prostate cancer at presentation after adjustment for differences in literacy, age, and city. They concluded that low literacy may be an overlooked but significant barrier to the diagnosis of early-stage prostate cancer among low-income white and black men.[103] Whether or not health literacy is related to breast cancer stage in women is relatively unknown.

Patient-Physician Communication

Communication is an essential clinical skill in medical oncology practice, and health literacy plays a key role in cancer patients' ability to discuss their disease with an oncologist in a meaningful way. Low health literacy influences both verbal and written communication between patients and their healthcare providers. There is often a mismatch between the way providers give out information and the way patients understand, remember, and apply the same information.[21,104] Oncologists and other health-care providers typically use information based on facts, probability, and their previous clinical

experience when discussing cancer treatment and prognosis with patients. However, the ability of patients to understand this kind of information is usually overlooked.

Furthermore, patients' emotional state during discussions of cancer diagnosis and treatment may also interfere with their understanding and recall of the information provided.[21] A study conducted by Davis et al. to analyze lifetime and 5-year breast cancer risk perceptions in 254 women aged 40 to 85 years showed that participants had a mean estimation error for lifetime and 5-year risk of 29.5 percent and 24.8 percent, respectively. These estimation errors were significantly correlated with lower numeracy rates.[105]

Many words that physicians consider to be "everyday language" may not be clearly understood by the general population.[106] Patients with low health literacy tend to be more responsive to information based on a health belief model where priority is given to patient action, motivation, and self-empowerment. Patients, especially those with low health literacy, are most interested in information that improves their sense of well-being and helps them resolve their immediate health problems.[107]

2.2.3 Health Literacy Measurement

Current instruments for measuring health literacy skill levels mainly capture an individual's ability to read. There is no gold-standard instrument to adequately assess the global health literacy concept by capturing the interactions of reading ability, numeracy, and oral literacy. The most commonly used instruments to measure health literacy are the Rapid Estimate of Adult Literacy in Medicine (REALM) and the Test of Functional Health Literacy in Adults (TOFHLA).[16] However, these instruments are lengthy and are not ideal for quickly identifying patients with limited health literacy in clinical practice. Consequently, other instruments like the Newest Vital Sign (NVS) have been designed for use in clinical practice.[17]

The REALM is a 66-item measure of health literacy which can be administered in 1-2 minutes by minimally trained personnel. It is used to assess whether an individual can correctly pronounce a series of health-related words listed in order of increasing difficulty. The REALM scores individual's health literacy on a continuous scale from 0-66. It has been validated as an instrument of reading ability and is highly correlated with traditional reading assessments.[108] Other versions of the REALM include a 7-item short form (REALM-SF),[109] an 8-item short form (REALM-R),[110] and a version for teens (REALM-Teen).[111]

The TOFHLA employs a different approach to measure health literacy, assessing both reading skills and numeracy. It consists of 17 items that measure numerical ability and three prose passages measuring reading comprehension. This health literacy instrument is not self-administered and takes up to 22 minutes to complete. For the reading comprehension, individuals are required to read health-related passages and fill in the blanks from a selection of four choices for each omitted word. Numeracy skills are assessed by asking a subject to respond to health-related prompts, such as pill bottle instructions and appointment slips.[112] The reading comprehension and numeracy subtests are highly correlated with each other ($r = 0.79$), and the TOFHLA as a whole is highly correlated with the REALM ($r = 0.84$).[112] The TOFHLA also has a short version (S-TOFHLA) which consists of four items to measure numeracy and two prose passages.[113]

The Newest Vital Sign (NVS) was developed by Weiss et al. in 2005 to assess the level of general health literacy in the primary care setting. The NVS uses an ice-cream nutrition label and six questions to assesses math, reading, and comprehension skills as well as abstract reasoning.

The NVS has good sensitivity and might be more sensitive than the TOFHLA to marginal health literacy.[17] In addition, its specificity is similar to or better than that of other

widely used clinical screening methods used to detect alcohol abuse,[114] detect arthritis,[115] measure osteoporosis risk,[116] and screen for breast cancer.[117] Despite the instrument's risk of overestimating the percentage of patients with limited literacy, it is a useful tool that can alert physicians to patients who may need more attention, and consequently help physicians pay more attention to improving physician-patient communication.[17]

Even though these instruments have good psychometric properties and are widely used, they were developed to measure general health literacy. Cancer patients are a unique subset of patients and these instruments would most likely be inadequate to accurately capture a cancer patient's ability to obtain, communicate, process, and understand cancer-specific health information and services needed to make appropriate health decisions. This led to the development of cancer-specific health literacy instruments in recent times.

Cancer Health Literacy Tool

In 2014, Dumenci et al. published an article describing the development of two cancer-specific health literacy instruments. One was designed to measure cancer health literacy along a continuum and the other was designed to identify patients with limited cancer health literacy. The instrument development process involved a mixed method approach. The qualitative phase was used to identify the boundaries of cancer health literacy to ensure comprehensive content coverage. A Delphi panel was employed to gain the insight into the perspectives of 11 health literacy scholars and clinicians, while six focus groups were conducted for 39 cancer patients to elicit their understanding of cancer health literacy. Each focus group had a balanced mix of males and females, as well as different ethnic groups. The groups were also stratified by the highest level of educational qualification.[18]

The list of cancer health literacy items which resulted from the qualitative phase was used to generate 76 items which were administered to 1,306 head and neck (26.2%), breast (16.3 %), skin (11.7%), genitourinary (10.3%) and other (35.5%) cancer patients. The data generated from this quantitative phase were used to create the final instruments as well as provide validity and reliability evidence. Thirty items resulted after examining exploratory factor analysis results, percentage of correct item responses, item-corrected total correlations, gender and race/ethnicity differences in item responses, and content coverage analysis. These 30 items make up the cancer health literacy tool (CHLT-30) which measures cancer health literacy along a continuum. Upon further statistical analysis, the six most informative items which could be used to identify individuals with limited cancer health literacy were used to form the second instrument, the CHLT-6.[18] The psychometric properties of these two instruments are discussed in more detail below.

Cancer Health Literacy Tool 30-item (CHLT-30)

The CHLT-30 instrument supports the unidimensional representation of cancer health literacy as a latent variable, with high precision. Total scores range from 0 – 30 with higher scores indicating higher health literacy. The mean raw CHLT-30 scores were 23.97 (+5.61), 24.26 (+5.19), 20.04 (+5.58), and 26.61 (+3.38) for men, women, non-Hispanic Blacks, and non-Hispanic Whites, respectively. External validation to determine the extent to which CHLT-30 scores predicted self-confidence about engaging in health decisions showed the CHLT-30 to be a significant predictor of self-confidence about engaging in health decisions ($p<.001$).[18]

The CHLT-30 has large discrimination parameters (mean=.84; median=.79; range=.49 to 1.36), as well as moderate to high item-corrected total correlations (mean=.42; median=.42; range=.31 to .54). Furthermore, the percent correct item responses were high

(mean=.81; median=.84; range=.56 to .93) and the item difficulty parameter estimates were all negative (p<.001; mean=-1.43; median=-1.53; range=-2.13 to -0.36), indicating that the items are relatively easy to answer. In addition, the CHLT-30 has excellent reliability characteristics, with a Cronbach's alpha of 0.88, 2-week test–retest reliability of 0.90, and 6-month test–retest reliability of 0.92. Furthermore, CHLT-30 scores showed no gender or racial/ethnic bias, even though Black patients' mean cancer health literacy score was significantly lower than that of Whites.[18]

In 2016, Echeverri et al. published a study describing the validation of a Spanish CHLT-30 version in 400 self-identified, Spanish-speaking, healthy Latinos. The majority of participants were from Central America (80.3%), between 25-55 years old (72.8%), and had a high school diploma or higher (61.8%). Study results were consistent with those obtained in the original validation study by Dumenci et al., 2014, confirming a unidimensional factor structure of the instrument. In addition, results showed similar internal consistency reliability estimates, and found significant differences in total scores by educational level. These results support the application of the Spanish CHLT-30 to assess cancer health literacy in healthy Spanish-speaking populations.[118]

Cancer Health Literacy Tool 6-item (CHLT-6)

The CHLT-6 is a cancer-specific health literacy tool which differentiates between patients with limited cancer health literacy and those with adequate cancer health literacy with a high degree of precision. It is highly correlated to the CHLT-30. The CHLT-6 can be used to differentiate between patients with limited CHL and those with adequate CHL based on responses to the six items. In the study by Dumenci et al., data from 1,306 cancer patients showed the average probability of belonging to the limited cancer health literacy class and adequate health literacy class to be 0.95 and 0.96, respectively in comparison to

a hypothetical gold standard probability of 1.0. This indicates that the accuracy of CHLT-6 is extremely high. There were also no gender or racial/ethnic biases found in the CHLT-6 scores. External validity analysis results showed that race/ethnicity, education, and income were significant predictors of whether or not an individual would have adequate cancer health literacy. Compared to individuals with adequate cancer health literacy, individuals with limited cancer health literacy were likely to be Black, under-educated, have low income, not be privately insured, and tended not to engage in health decisions.[18]

2.3 Patient Activation

Patient engagement is a broad concept that includes patient activation, the interventions designed to improve patient activation, and patients' behavior as result of such interventions. Patient activation itself, refers to a patient's understanding of his/her role in the healthcare process and the possession of knowledge, confidence, and skills to facilitate active participation in managing their health. This motivates a patient to become engaged by taking preventive actions, collaborating with providers, managing symptoms and problems, and finding and using high-quality and appropriate care.[22-24] Patient activation is a measurable intermediate outcome of care that is linked with health outcomes.[22]

2.3.1 Patient Activation Measure (PAM)

Patient activation is not a dichotomous variable that either exists or does not exist in different patients. It is a latent construct that can be measured on a continuous scale using the patient activation measure (PAM), and it changes over a patient's life course.

The PAM is a series of questions that estimate an individual's self-concept as a manager of his or her health and health care, with response options that are degrees of

agreement or disagreement. It was developed by Hibbard et al. in the early 2000s and is an interval-level, developmental, unidimensional, and probabilistic Guttman-like scale. The PAM enables the assessment of an individual's knowledge, skills, beliefs and confidence for managing his or her health and healthcare.[24,25]

The PAM was originally designed as a 22-item Guttman-scale with four levels of activation. It measures the confidence, knowledge, and skills that patients have to manage their health/health condition(s). In the first activation level, patients take no active steps to be involved in their healthcare. In the second activation level, patients possess the knowledge and have confidence to be partners in managing their health but take no action. In the third activation level, patients are proactive in maintaining and improving their health. In the fourth activation level, patients remain partners in managing their health even when faced with stress.[24]

In 2005, Hibbert et al. developed a 13-item short form of the original PAM. The scores on this shorter version were identical to those from the 22-item version ranging from 38.6 to 53.0 on a theoretical 0 to 100-point scale. Like the 22-item measure, this short version was designed to be used in a clinical setting and its infit and outfit values also fell between the acceptable range of 0.5 to 1.5. However, there was some loss of precision with the 13-item version, which showed a lower reliability for individuals without chronic diseases, those 85 years and above, those with lower socioeconomic status and those with self-rated poor health. However, these lower scores still fell within the acceptable range.[31] In addition to its usefulness in determining activation levels, the PAM can also be employed to evaluate tailored interventions designed to move patients from one level of activation to another.[24]

PAM Psychometric Properties

The psychometrics of this scale, when tested in a convenience sample of 486 individuals (n = 118 without chronic disease), showed comparable reliability statistics for those with disease and without disease. The Rasch analysis was used to test the psychometric properties of this instrument. In this analysis, item selection is based on item fit statistics which represent how much the item responses deviate from the model's expectations. The infit value is most sensitive to item fit for an item whose scale location is close to the respondent's location, while the outfit value is more sensitive to item fit when an item's scale location is distant from the respondent's scale location. Item fit values between 0.5 and 1.5 indicate sufficient unidimensionality and expected response variability for a rating scale measurement.[24]

The items in the PAM scale had infit values (0.76 to 1.32) which were within the range for a unidimensional measure. The 22-item Rasch person reliability ranged from 0.85 (real) to 0.88 (model) and the Cronbach's alpha was 0.91. The PAM also showed a high level of reliability when further testing was done in a national probability survey (N = 1,515). Infit values ranged from 0.71 to 1.44 while the outfit statistics (except one) ranged from 0.80 to 1.34. In addition, the PAM had high degrees of construct and criterion validity.[24]

2.3.2 Patient Activation and Health Outcomes

Activated patients understand that apart from the care and support of medical practitioners, the sustenance of good health depends on their knowledge of their disease condition, the possession of skills to manage their symptoms and the confidence to take appropriate action when necessary.

Patients with low activation are twice as likely to delay medical care, and three times more likely to have unmet medical needs in comparison to patients with high activation.[29] In addition, patients that are highly activated are at least two times as likely to prepare questions for a physician visit, to know about treatment options for their disease, to seek health information, and to compare the quality of health care received from providers compared to patients with low activation.[30,31] Challenging behaviors are less likely to be adopted by patients with low activation, therefore, tailoring interventions to patients' activation level by encouraging realistic behavior has a greater chance of successfully increasing their level of activation.[23]

Studies have provided evidence that patients who have high activation levels have better health outcomes and place a lower burden on the health system with fewer hospitalizations and less emergency department visits.[25-28] Patient activation is a modifiable factor and interventions tailored to individual patients' activation level have been shown to be effective in increasing patient activation. However, patients with the lowest activation tend to have greater improvements in activation when interventions are introduced compared to patients who already have high activation levels (ceiling effect).[22,32-34]

Compared to Caucasians and African Americans, Hispanics have much lower levels of patient activation with only 24.8 percent of Hispanics at the highest level of patient activation (activation level 4), compared to 39.5 percent of blacks and 45.3 percent of whites. Low acculturation and ability to navigate the American healthcare system have been identified as contributory factors to these differences which persist even after controlling for other demographic and socioeconomic factors. In addition, Hispanic breast cancer patients have the greatest odds for decision dissatisfaction and are more vulnerable to poor breast cancer treatment decision outcomes than patients of other ethnicities.

Consequently, increased patient activation among this patient population might significantly reduce disparities in their access to healthcare.[35,36]

Irrespective of disease type and economic level, highly activated patients have greater adherence to treatment regimens and are more likely to regularly perform self-monitoring as well as obtain regular chronic disease care.[25,31,37-39] A number of studies have examined the impact of improved activation in patients with different chronic diseases such as diabetes, depression, HIV and hypertension and the results of these studies show the financial, clinical, and psychological benefits of such interventions.[40-42]

2.3.3 Patient Activation in Chronic Disease States

In a 2013 study, Marshall et al. investigated the association between patient activation and health outcomes in HIV-infected individuals. The cross-sectional study was conducted among 433 patients in four different clinics using the 13-item PAM, CD4 counts, viral load counts and patient-reported adherence. Study results revealed that patient activation was high overall, with an average PAM score of 72.3$\pm$ 16.5. Multivariate models showed that every 5-point increase in PAM scores was associated with greater odds of adherence, viral suppression and CD4 count >200 cells/ml. They concluded that patient activation improved patient adherence and consequently led to more efficient viral suppression.[41]

In another study, Kukla et al. also studied the relationship between patient activation and disease outcomes in schizophrenic patients. A total of 119 patients were enrolled in a randomized control trial for 18 months. Patient activation was measured using the 13-item mental health version of the PAM, psychiatric symptoms were measured using the 30-item Positive and Negative Syndrome Scale (PANSS) and medication adherence was measured with the 4-item Morisky scale. The mean PAM score of study participants

was moderate (55.6 $\pm$ 16.0). The results revealed that positive recovery attitudes, higher levels of hope and fewer emotional discomfort symptoms were associated with higher patient activation scores. However, there was no link between medication adherence and patient activation in this group of patients.[119]

A systematic review conducted by Kinney et al. revealed an inverse relationship between patient activation scores and hospitalizations.[120] In particular, chronic cardiopulmonary disease patients had increasingly higher rates of 30-day post discharge re-hospitalization as activation scores decreased. Compared with activation level 4 patients (highest activation scores), patients in activation level 3, 2, and 1 had 1.30, 1.50, and 1.75 times higher rates of re-hospitalization, respectively. A similar trend was also revealed for emergency department visits.[27,120,121]

Remmers et al. also investigated the ability of PAM scores to predict future health outcomes in diabetes patients, using a multivariate logistic regression. Study results revealed that the PAM was predictive for hemoglobin A1c testing, low-density lipoprotein cholesterol (LDL-C) testing, and hemoglobin A1c control. However, it was not predictive for lipid lowering drug use, LDL-C control or acute myocardial infarction discharges. They concluded that patients at risk for poorer health outcomes could be identified using PAM scores.[26]

Lastly, O'Malley et al. investigated the determinants of patient activation in a predominantly Caucasian (77%) and African American (15%) cohort of breast and prostate cancer survivors. The response option of the PAM was modified to range from 1 to 4 with higher scores indicating greater patient activation. The study results revealed that among the 213 breast cancer survivors, overall patient activation was high with a mean of 3.34±0.37 and this was significantly higher than that of the 112 prostate cancer survivors (3.25±0.38). Race, marital status, employment status, household income, and fear of

recurrence were significantly associated with patient activation for only prostate cancer survivors. However, for both breast and prostate cancer survivors, ease of access to and perceptions of time spent with healthcare providers (oncology team and primary care physicians) were positive predictors of activation.[43]

Patient activation has also been shown to affect the behaviors and experiences of cancer survivors. Highly activated cancer survivors are more likely to feel that values are reflected in their treatment plans and they are more likely to adequately handle side effects than less activated patients. On the other hand, less activated patients are less likely to understand their diagnosis, follow treatment regimens, or be satisfied with their care.[122]

2.3.4 Health Literacy and Patient Activation

Patient activation and health literacy are independent predictors of health and deficits in either of them could serve as targets for behavioral intervention.[44,45] Higher activation helps individuals with low literacy and numeracy abilities to compensate for their lower skills and to achieve higher levels of comprehension. When health trade-offs are necessary, making the right choice depends on literacy and comprehension as well as patient activation.[46]

A study by Hibbard et al. investigating the relationship between patient activation and health literacy showed that among older adults, both health literacy and patient activation were significantly and positively related to healthcare decision making, even though this relationship was stronger for health literacy. Patient activation had slightly stronger relationships to health-care-related behaviors, healthy behaviors, and self-management behaviors than health literacy.[47] Another study by Nijman et al. which examined the relative contribution of patient activation and functional health literacy to the seeking and use of health information showed that more activated consumers were more

likely to seek and use health information. In the study sample, health literacy increased as patient activation increased, with a weak to moderate overall correlation between the health literacy and activation scores.[48]

Recent studies in oncology reveal that health literacy and certain aspects of patient activation are correlated. A cross-sectional, multicenter oncology study examined patient activation, health literacy, symptom burden, confidence to self-manage side effects, and medication adherence to oral oncolytics. Results showed that confidence to self-manage side effects (e.g., fatigue and diarrhea) were associated with higher health literacy and higher patient activation.[49] Another study revealed that higher patient activation increases colorectal cancer screening in low income, minority patients with limited health literacy skills.[50] However, these studies were conducted in homogenous patient populations (95% Caucasian), were not specific to breast cancer patients, or did not illustrate the relationships of patient activation and health literacy to health outcomes and resource utilization.

2.4 Theoretical framework

The health literacy skills (HLS) framework put forth by Lee et al. in 2004 will be used in this study.[123] The HLS framework (Figure 2.1) describes how health literacy affects health outcomes through intermediate factors. It also depicts the net effects of health literacy and intermediate variables. The intermediate factors linking health literacy to health outcomes include disease and self-care knowledge, health risk behavior, preventive care and physician visits, and compliance with medications. The health outcomes are health status, emergency care, and hospitalization, while the moderators/control variables include gender, ethnicity, socioeconomic status, health insurance coverage, disease severity, and income.[123]

Specifically, the HLS framework posits that individuals with lower health literacy are likely to have poorer medical knowledge, worse health behavior, less regular preventive care and physician visits, and poorer compliance with routine clinical visits and medications. These factors, in turn, may delay seeking timely and appropriate care, produce poor health outcomes, and increase the use of emergency and hospital services. In testing the relationships between variables, important confounders including socioeconomic status, educational level, age, gender, ethnicity, health insurance coverage, disease severity, and income serve as control variables.[123]

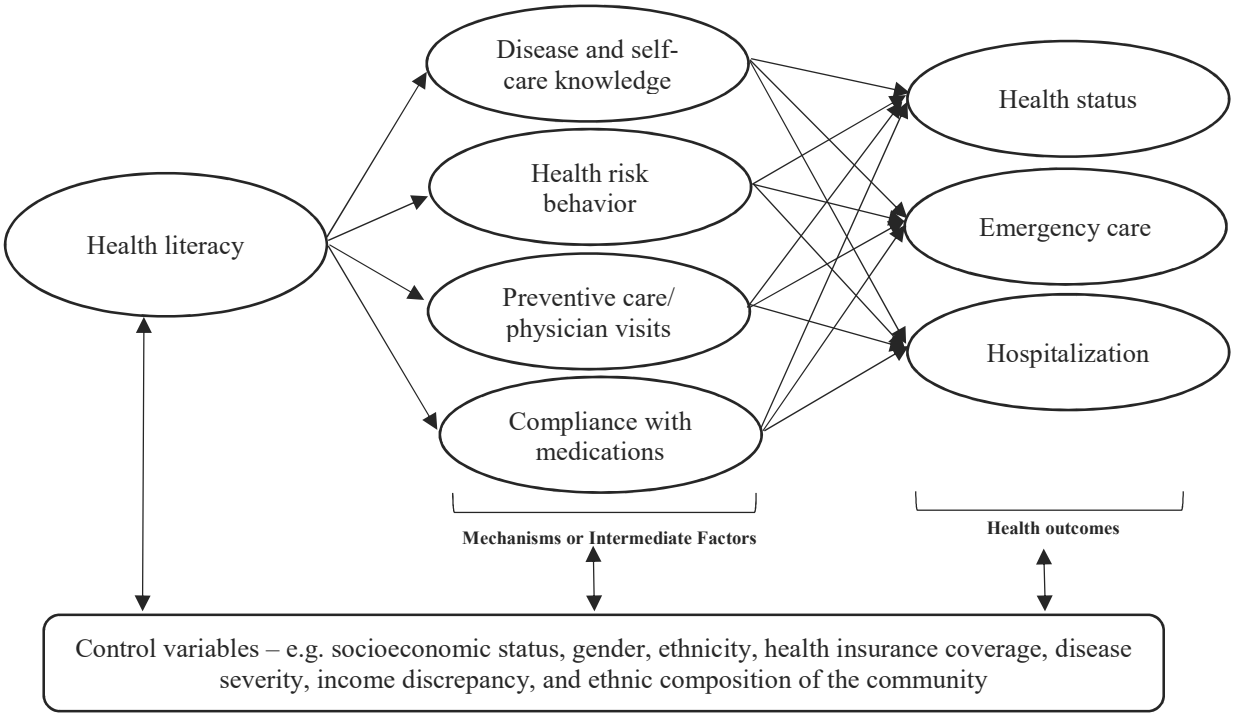


Figure 2.1: Health Literacy Skills Framework[123]

Studies have consistently shown that patients with diabetes, asthma, hypertension, HIV/AIDS, and cancer who have low health literacy are less knowledgeable about their disease and less capable of adequate self-care.[102,124-126] Furthermore, such patients with less knowledge of disease management are likely to have lower health status and suffer from more severe illnesses, leading to more emergency department visits and hospitalizations.[123] Increasing health literacy tends to improve self-reported health status, lower healthcare costs, increase health knowledge, shorten hospitalizations, and decrease use of healthcare services.[88,127-129]

Cho et al. explored disease knowledge, health behavior, preventive care, and compliance as potential intermediate factors which could link health literacy with health status and utilization. Study participants consisted of 489 elderly Medicare patients who completed face-to-face interviews between March 2003 and February 2004. The majority of participants were female (78.7%), African American (59.1%), and had an average education equivalent to a high school diploma. Health literacy was measured using the Short Test of Functional Health Literacy in Adults (S-TOFHLA) and 29 other items measured disease knowledge, health behavior, preventive care, medication compliance, and health status. Health care utilization was assessed by asking participants the number of emergency room visits and the number of hospital admissions they had in the previous year. Study results showed that health literacy was significantly and positively correlated with health status ($r = 0.50$) as well as the four intermediate factors of disease knowledge ($r = 0.38$), health behavior ($r = 0.42$), preventive care ($r = 0.21$), and medication compliance ($r = 0.20$). Conversely, health literacy was negatively correlated to healthcare utilization.[130]

Another study by Halverson et al. examined the association of HRQoL and health literacy among a registry-based statewide sample of 1,841 newly diagnosed breast, lung,

prostate, and colorectal cancer patients in Wisconsin. Sociodemographic and clinical data were obtained from the state's cancer registry, while health literacy and HRQoL were measured with a mailed questionnaire consisting of a cancer-specific quality of life instrument (FACT-G) and four self-report items measuring health literacy on a 5-point Likert scale. The survey respondents were mostly non-Hispanic Whites (93%) and female (50.8%) with a mean age of 63.2 (±10.7). Study results showed that higher health literacy was significantly associated with greater HRQoL. Controlling for covariates, there were also significant differences between those in the highest and lowest health literacy categories and in the four quality of life subscales (physical, functional, emotional, social) of the FACT-G. They concluded that health literacy is positively and independently associated with HRQoL among cancer patients. Such findings suggest the need to take the health literacy level of cancer patients into account in the course of disease management as tailored communication regarding the risks and benefits of tests and treatments may be beneficial in this population.[11] Other health outcomes resulting from higher health literacy included patient acquisition of new knowledge, more positive attitudes, greater self-efficacy, and positive health behaviors.[131]

It has been hypothesized that health literacy influences health outcomes through three main mechanisms:[132]

- Healthcare access and utilization which are influenced by navigation skills, self-efficacy and perceived barriers.
- Patient-provider interactions which are influenced by knowledge, beliefs and participation in decision-making.
- Self-care which is influenced by motivation, problem-solving, self-efficacy, knowledge, and skills.

The factors that influence self-care are embodied in patient activation, which is a compound construct that represents the confidence, knowledge, and skills that individuals have to manage their health and healthcare.[133] Therefore, disease self-care/knowledge, a key component of patient activation, is the intermediate factor of interest in the proposed model. Patient activation has been shown to mediate the relationship between health literacy and health outcomes.[134] The influence of health literacy on the outcome variables via patient activation, controlling for covariates, will be investigated in this study. Figure 2.2 depicts the specific framework that will be employed.

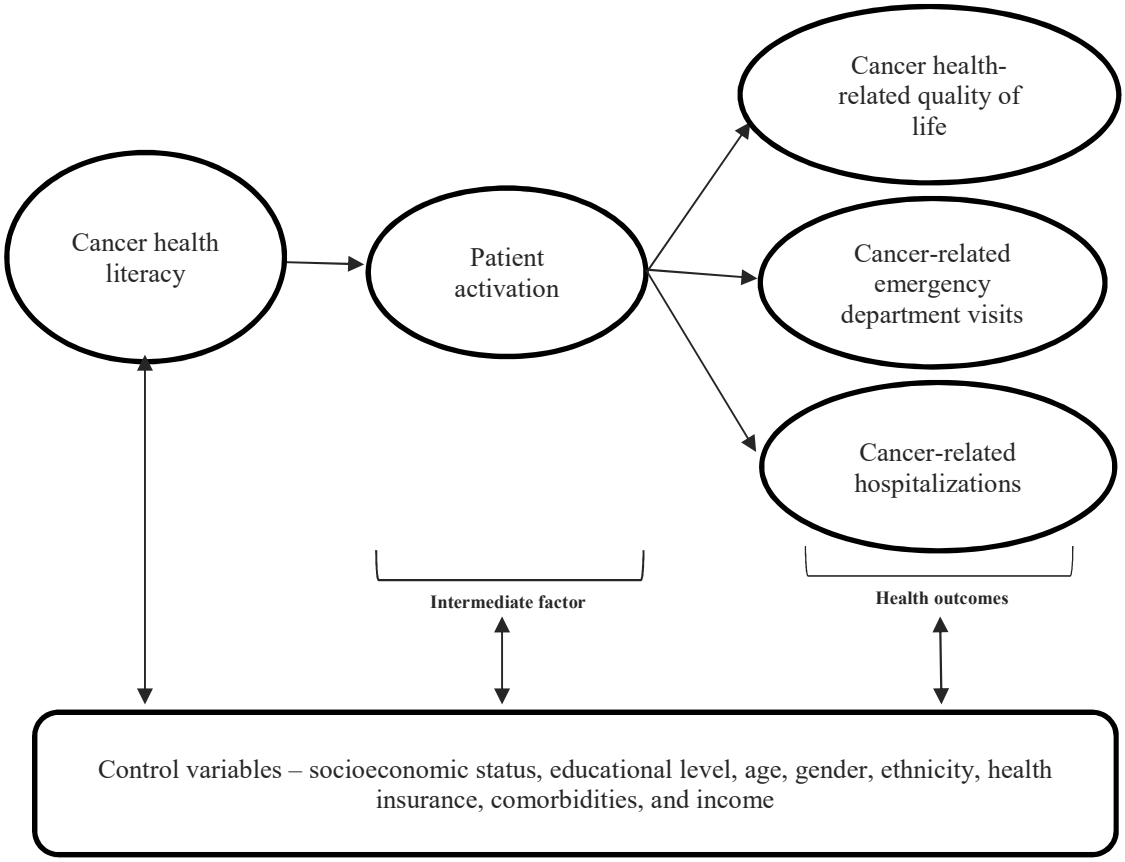


Figure 2.2: Health Literacy Skills Framework in Breast Cancer Patients

2.5 Study significance

Compared to individuals with poor health literacy levels, those with high health literacy have significantly lower predicted values of office visit expenditures ($719 vs $1,284) and emergency department visit expenditures ($100 vs $151).[135] Also, patients with high activation levels have better health outcomes and place a lower burden on the health system with fewer hospitalizations and less emergency department visits.[25-28] However, only a few studies have examined the relationship of both patient activation and health literacy with health outcomes to date,[44,47] and no known studies have investigated this relationship in breast cancer patients.

Health literacy is closely related to an individual's ability to use information to make health-related decisions while patient activation is more closely aligned with health outcomes such as chronic disease self-management. Though similar, both constructs are unique predictors of health[47]

The majority of studies that have examined health literacy and patient activation in breast cancer patients have primarily focused on disease screening/detection. The common instruments (REALM and TOFHLA) used to assess health literacy in cancer patients primarily assess reading proficiency and word recognition. In addition, there is little evidence of the association between TOFHLA or REALM scores and cancer patient engagement in health decisions.[18,136] This is a major limitation of these instruments because the ability to make appropriate health decisions is the primary outcome of health literacy. Also, these instruments are probably not sensitive to cancer-specific literacy because of the complex treatment choices that cancer patients face, coupled with the increased demand for self-care.[18,87,136]

Furthermore, the only known study that has investigated patient activation in cancer survivors used a mixed population of breast and prostate cancer survivors to assess rates

of patient activation as well as explore the demographic and clinical characteristics associated with activation in the population.[43] There is still an unmet need to assess health literacy in patients with a confirmed breast cancer diagnosis using a cancer-specific instrument and also to examine its association with patient self-ability to manage health and breast cancer-relevant health outcomes. In addition, it might be useful to explore how the recently developed cancer-specific health literacy tool (CHLT-6) compares with a general health literacy instrument (NVS) that assesses math, reading, and comprehension skills as well as abstract reasoning, and whose specificity is comparable to that of widely used health literacy measures.

The aim of this study was to assess health literacy and patient activation in HER-2 positive breast cancer patients as well as examine their relationships to health outcomes. The findings of this study could inform and facilitate the provision of activation level-appropriate information to breast cancer patients at their literacy level, thereby increasing the effectiveness of interventions to improve patients' involvement in managing their health. This would enhance the ability of health care providers and policy-makers to personalize the delivery of care for breast cancer patients, resulting in improved quality of life and less utilization of limited healthcare resources.

Chapter 3: Methodology

The purpose of this study was to assess cancer health literacy and level of patient activation in a sample of HER-2 positive breast cancer patients as well as examine the relationship between these two constructs and their influence on health outcomes. This chapter outlines the study design, study objectives and hypotheses, study variables, study sample, enrollment protocol, data collection, and statistical analyses.

3.1 Study Design

A prospective, cross-sectional study design was used to achieve the study objectives. A single survey consisting of 67 items (Appendix 1) was used to collect data from HER-2 positive breast cancer patients receiving chemotherapy in selected Texas-based oncology clinics. HER-2 positive breast cancer patients were the target study sample because they typically have office visits for the receipt of chemotherapy and/or targeted therapy treatment. Therefore, these patients could participate in the study during their office visits.

The selected oncology clinics are part of a larger practice consisting of over 460 physicians in 210 locations throughout Texas and southeastern Oklahoma. In addition to adopting a community-based approach to oncology care, this practice participates in value-based care models, including the Oncology Care Model (OCM), which are designed to improve patient care and the cancer treatment experience. These care models help patients to better understand their illness and treatment, manage treatment side effects, and avoid unnecessary hospital and emergency room visits.[137,138]

The survey used in this study was pre-tested with three breast cancer patients. During regular clinic visits, eligible patients were offered participation in the study by

clinic staff. Patients who give their consent to participate were asked to complete a self-reported survey (Appendix 1) consisting of the 6-item cancer health literacy tool (CHLT-6), the 6-item newest vital sign (NVS), the 13-item patient activation measure (PAM 13), the 27-item functional assessment of cancer therapy (FACT-G v. 4), two items measuring the quality of patient-provider communication, and single item measures for the number of breast cancer-related emergency department visits, and hospitalizations, as well as clinical and demographic patient characteristics.

3.2 Study objectives and hypotheses

The objectives of this study and corresponding hypotheses are as follows:

1. To describe health literacy, patient activation, clinical (stage of breast cancer at diagnosis, time since diagnosis, type of breast cancer treatment received, comorbidities) and demographic (age, gender, educational level, ethnicity, household income, insurance status, marital status) characteristics of a breast cancer patient sample.
2. To examine the relationships between health literacy and clinical and demographic characteristics in a sample of breast cancer patients.
3. To examine the relationships between patient activation and clinical and demographic characteristics in a sample of breast cancer patients.
4. To assess the relationship between cancer health literacy and patient activation in a sample of breast cancer patients.

   H1: Breast cancer patients who have adequate cancer health literacy will have higher patient activation compared to those that have limited cancer health literacy.
5. To examine the relationship between cancer health literacy and patient-provider communication in a sample of breast cancer patients.

H2: Breast cancer patients who have adequate cancer health literacy will have easier patient-provider communication and understanding of information provided compared to those that have limited cancer health literacy.

6. To assess the relationship between cancer health literacy and general health literacy in a sample of breast cancer patients.

   H3: There will be a significant positive relationship between cancer health literacy and general health literacy in the sample of breast cancer patients.

7. To determine the overall predictive validity of the health literacy skills (HLS) framework in explaining health outcomes (cancer health-related quality of life, cancer-related emergency department visits, and cancer-related hospitalizations) using cancer health literacy and patient activation, controlling for cancer health literacy X patient activation interaction and clinical/demographic characteristics.

   H4: Cancer health literacy and patient activation will explain a significant amount of variance in cancer health-related quality of life controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

   H5: Cancer health literacy and patient activation will explain a significant amount of variance in cancer-related emergency department visits controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

   H6: Cancer health literacy and patient activation will explain a significant amount of variance in cancer-related hospitalizations controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

8. To predict cancer health-related quality of life in breast cancer patients using cancer health literacy and patient activation controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

   H7: Cancer health literacy and patient activation will be significant positive predictors of cancer health-related quality of life controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

9. To predict cancer-related emergency department visits in breast cancer patients using cancer health literacy and patient activation controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

   H8: Cancer health literacy and patient activation will be significant negative predictors of cancer-related emergency department visits controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

10. To predict cancer-related hospitalizations in breast cancer patients using cancer health literacy and patient activation controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

    H9: Cancer health literacy and patient activation will be significant negative predictors of cancer-related hospitalizations controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics.

3.3 Study Variables

The primary independent variable in this study is cancer health literacy while patient activation is the secondary independent variable. Dependent variables include cancer health-related quality of life, number of cancer-related ED visits, number of cancer-related hospitalizations, and quality of patient-provider communication. Measures for each variable are discussed in detail below.

3.3.1 Independent Variables

Cancer Health Literacy (CHL)

Health literacy is defined as the degree to which an individual can obtain, communicate, process, and understand basic health information and services needed to make appropriate health decisions.[87] The 6-item cancer health literacy tool (CHLT-6) is a cancer-specific health literacy tool which was developed by Dumenci et al. in 2014 to measure the health literacy of cancer patients (items 1 – 6 in Appendix 1).[18]

The CHLT-6 can be used to differentiate between patients with limited CHL and those with adequate CHL based on responses to the six items. Each item has only one correct response option which is scored as one while incorrect option(s) are scored as zero. There are 64 possible response patterns for the six items and each pattern has a specific probability of adequate and inadequate CHL, which sum up to unity. A patient's CHL is identified by choosing the CHL with the higher probability based on his or her response pattern. For example, a response pattern of 001001 to the six items has a 0.88 probability of limited CHL and a 0.12 probability of adequate CHL. Therefore, patients with this response pattern will be considered to have limited CHL. On the other hand, a response pattern of 111011 to the six items has a 0.17 probability of limited CHL and a 0.83

probability of adequate CHL. Therefore, patients with this response pattern will be considered to have adequate CHL.[18]

During its development, data from 1,306 cancer patients showed the average probability of belonging to the limited CHL class and adequate CHL class to be 0.95 and 0.96, respectively. Compared to the hypothetical gold standard probability of 1.0, this indicates that the accuracy of CHLT-6 is extremely high. The large differences in the probability of correct responses to the six items between adequate and limited CHL classes also indicate that the CHLT-6 separates patients with limited CHL from those with adequate CHL with a high degree of precision.[18]

In addition, there were no gender or racial/ethnic bias found in CHLT-6 scores for this sample. Multigroup latent class analysis was used to test gender and racial/ethnic bias. Results supported the measurement invariance in both gender and racial/ethnic groups, providing evidence that CHLT-6 scores were free from bias. External validity analysis results also showed that race/ethnicity, education, and income were significant predictors of whether or not an individual would have adequate CHL.[18]

General Health Literacy

The Newest Vital Sign (NVS) was developed by Weiss et al. in 2005 to assess the level of general health literacy in the primary care setting. The NVS uses an ice-cream nutrition label and six open-ended questions to assesses math, reading, and comprehension skills as well as abstract reasoning (items 7 – 12 in Appendix 1).[17] This instrument takes approximately three minutes to be administered either face-to-face or in the paper/pencil format.[17,139,140] Total scores range from 0 to 6 with higher scores indicating higher general health literacy. Patients who answer at least four questions correctly on the NVS are considered to have adequate health literacy while those who answer less than four questions

correctly most likely have limited health literacy. The NVS has good sensitivity and might be more sensitive than the TOFHLA to marginal health literacy. In addition, its specificity is similar to or better than that of other widely used clinical screening methods.[17]

Patient Activation

Patient activation is defined as the confidence, skill and knowledge that patients possess which determine the level of their participation in managing their disease. It is measured using the patient activation measure (PAM) which categorizes patients into four levels of activation based on their total score.[133] The PAM is an interval level, unidimensional, 13-item instrument which measures a patient's willingness and ability to manage his/her health and healthcare (Figure 3.1). It has been shown to be a highly reliable and valid instrument. Rasch analysis shows that the 22-item PAM scale has infit (0.71 to 1.44) and outfit (0.80 to 1.34) values within the normal range of 0.5 to 1.5. Also, the 22-item Rasch person reliability ranges from 0.85 (real) to 0.88 (model) and the Cronbach's alpha is 0.91. The psychometric scores of the 13-item scale are similar to that of the 22-item version. The PAM-13 items have a calibrated scale range from 38.6 to 53.0, which is comparable with the PAM-22 item range of 38.3 to 54.5. The infit and outfit statistics for the PAM-13 items also fall within the acceptable scale range of 0.5 to 1.5. The statistically significant relationships ($p<0.001$) between the PAM scores and conceptual variables (such as preventive behaviors, disease-specific self-management behaviors, and consumeristic behaviors) are evidence of the scale's construct validity.[133,141]

Patient activation as outlined in the PAM involves four progressive levels of patient activation (Figure 3.1). Patients in activation level 1 usually do not feel in charge of their own health. These patients tend to lack basic knowledge about their condition as well as confidence in their ability to manage their health. Increasing these patients' activation level

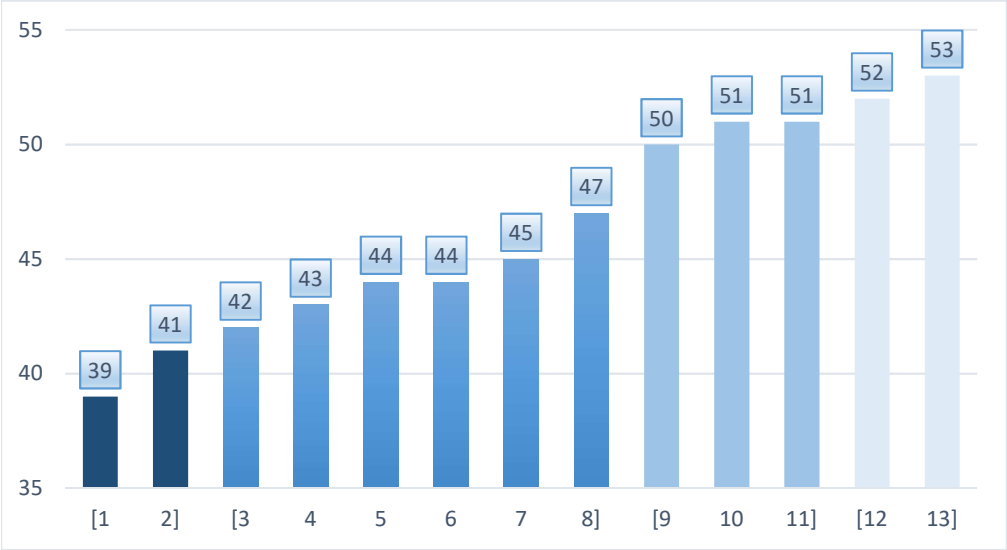
involves getting them to realize that they have an active role to play in managing their health.

Patients in activation level 2 tend to have some knowledge about their condition, treatment options, and/or self-care, even though large gaps remain. These patients have little experience or success with behavior change. Increasing activation in level 2 patients involves improving their knowledge of their disease condition and its management, as well as increasing their confidence to take action when symptoms arise.

Activation level 3 patients generally understand the key facts of their condition and treatment as well as some experience and success in making behavioral changes. They also have some confidence in handling limited aspects of their health. Increasing activation in this level involves increasing patients' confidence and ability to manage all aspects of their illness by building on their past experience and successes

Patients in activation level 4 have typically made most of the necessary behavior changes with regards to managing their health but may have difficulty in being consistent over time, or during times of stress. For these patients, it is important to increase their confidence and skills for maintaining behaviors and coping with stress, even in the presence of routine stressors or when there is a change in their disease severity.

Item scale locations can be converted from the original scale to a theoretical 0–100 point scale using the PAM-13 scoring spreadsheet. Total scores on the 13-item PAM range from 38.6 to 53.0, with higher scores signifying greater activation.[141] See Appendix 1, items 13 to 25 for the scale items.



Key: Item calibrations are the calibrated scale value of the item.

Figure 3.1: Patient Activation Measure with Item Calibrations and Four Activation Levels Identified

3.3.2 Dependent Variables

Health-Related Quality of Life (HRQoL)

HRQoL is a multi-dimensional concept that measures an individual's perception of his or her own health. It includes physical, mental, emotional, and social functioning domains which collectively describe the impact of health status on quality of life.[142] The functional assessment of cancer therapy, general version 4 (FACT-G v. 4) is considered to be a standard assessment of HRQoL in cancer patients. This self-administered instrument consisting of 27 items (items 26 – 52 in Appendix 1) measures quality of life over the last seven days pertaining to four areas:[143,144]

1. Physical well-being – 7 items
2. Social/family well-being – 7 items
3. Emotional well-being – 6 items
4. Functional well-being – 7 items

Responses to each item are on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much) with higher numbers indicating a better health state. Scores can be generated for each sub-scale provided that more than 50 percent of the items comprising the subscale are answered. A subscale score is computed as the prorated sum of the item responses for that subscale. Missing values are replaced with the mean of completed items for that subscale. Subscale scores range from 0 – 28 for physical, social/family, and functional well-being, while emotional well-being scores range from 0 – 24. The FACT-G v. 4 total score ranges from 0 – 108 and is computed as the sum of the four subscale scores, provided that at least 80 percent of the 27 items were answered. Negatively worded items are reverse scored prior to summing so that higher subscale and total scores indicate higher HRQoL.[145,146]

The original FACT-G version was validated in a mixed cancer patient population that included breast, colorectal, and lung cancer patients. It has evidence of reliability, validity, and responsiveness. In addition to test-retest reliability and responsiveness, it can discriminate between patients based on disease stage, performance status rating, and hospitalization status. It is sensitive to change over time and compares well to other scales measuring similar constructs like the Functional Living Index of Cancer (FLIC) and Eastern Cooperative Oncology Group (ECOG) performance status rating. There is also differential responsiveness of the FACT-G subscales to groups that differ in physical, social, emotional, and functional well-being. [143]

Number of Cancer-Related Emergency Department (ED) Visits

One open-ended item was used to measure how often patients sought emergency medical care due to breast cancer complications in terms of the number of ED visits in the last 30 days: Within the last 30 days, how many times have you had to visit the emergency department due to a breast cancer complication?

Number of Cancer-Related Hospitalizations

One open-ended item was used to measure how often patients were hospitalized due to breast cancer complications in the last 30 days: Within the last 30 days, how many times have you been hospitalized due to a breast cancer complication?

Quality of Patient-Provider Communication

Two items with five response options on a Likert scale were used to assess the quality of patient-provider communication: 1) How difficult is it for you to communicate your concerns about your breast cancer to your healthcare provider(s); and 2) How difficult is it for you to understand the information provided by your healthcare provider(s) about your breast cancer?

3.3.3 Patient Demographic and Clinical Variables

Single items were used to measure the demographic and clinical characteristics of study participants. Age, gender, educational level, ethnicity, household income, insurance status, marital status, stage of breast cancer at diagnosis, type(s) of breast cancer treatment(s) received, time since diagnosis, and comorbidities.

Table 3.1 contains a summary of all the variables that were used in the study, their operational definitions and the number of items that measured each variable.

Table 3.1: Constructs and Operational Definitions

Construct	Operational definition	Item(s)
Independent variables		
Cancer health literacy	The 6-item cancer health literacy tool (CHLT-6) was used to measure cancer health literacy. Individuals were considered to have adequate or limited cancer health literacy based on their responses to the six items.	6
General health literacy	The 6-item newest vital sign (NVS) was used to measure general health literacy. Patients who answered three or fewer questions correctly were considered to have limited health literacy while those that answered more than three questions correctly were considered to have adequate health literacy.	6
Patient activation	The 13-item patient activation measure (PAM) was adapted to measure disease and self-care knowledge/ability in breast cancer patients. Total PAM scores range from 0 to 100 with higher scores indicating greater patient activation. Patients were grouped into four levels of activation based on their PAM scores: Activation level 1 ($\leq$ 41) coded as 1 Activation level 2 ($\geq$ 42 but < 50) coded as 2 Activation level 3 (50 – 51) coded as 3 Activation level 4 ($\geq$ 52) coded as 4	13
Dependent variables		
Cancer health related quality of life (HRQoL)	The 27-item FACT-G was used to measure cancer HRQoL in four subscales: 1. Physical well-being – 7 items 2. Social/family well-being – 7 items 3. Emotional well-being – 6 items 4. Functional well-being – 7 items Responses to each item were on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much) with higher scores indicating greater HRQoL. Subscale scores ranged from 0 – 28 for physical, social/family, and functional well-being, while emotional well-being scores ranged from 0 – 24. Total FACT-G score ranges from 0 – 108.	27

Table 3.1: Constructs and Operational Definitions Contd.

Construct	Operational definition	Item(s)
Number of cancer-related emergency department visits	One open-ended question was used to measure this construct: Within the last 30 days, how many times have you had to visit the emergency department due to a breast cancer complication? …….. times	1
Number of cancer-related hospitalizations	One open-ended question was used to measure this construct: Within the last 30 days, how many times have you been hospitalized due to a breast cancer complication? …….. times	1
Quality of patient-provider communication	Two questions were used to measure the quality of patient-provider communication. Responses to each item were on a 5-point Likert scale ranging from 1 (extremely difficult) to 5 (extremely easy): How difficult is it for you to communicate your concerns about your breast cancer to your healthcare provider(s)? 1 = Extremely difficult 2 = Somewhat difficult 3 = Neither easy nor difficult 4 = Somewhat easy 5 = Extremely easy Higher scores indicated easier patient communication with healthcare provider(s)	1
	How difficult is it for you to understand the information provided by your healthcare provider(s) about your breast cancer? 1 = Extremely difficult 2 = Somewhat difficult 3 = Neither easy nor difficult 4 = Somewhat easy 5 = Extremely easy Higher scores indicated easier patient understanding of information	1
Covariates		
Age	Year of birth (subtracted from 2018)	1

Table 3.1: Constructs and Operational Definitions Contd.

Construct	Operational definition	Item(s)
Gender	One question with four nominal response options was used to measure this construct: What is your gender? 1 = Male 2 = Female 3 = Transgender 4 = Other (please specify)	1
Educational level	One question with four ordinal response options was used to measure this construct: Which option best describes your highest education level? 1 = Less than High School 2 = High School Graduate or GED 3 = College graduate 4 = Postgraduate (e.g., MD, MS, PhD) Higher scores indicated a higher educational level	1
Ethnicity	One item with six nominal response options was used to measure this construct: Which of the following best describes your racial/ethnic background? 1 = African-American or non-Hispanic black 2 = American Indian or Alaska Native 3 = Asian-American or Pacific Islander 4 = Caucasian or non-Hispanic white 5 = Mexican-American or Hispanic 6 = Other (please specify) ……	1
Household income	This construct was measured by a single item with five ordinal response options: Which option best describes your annual household income? 1= Less than $25,000 2 = $25,000 to $50,000 3 = > $50,000 to $75,000 4 = > $75,000 to $100,000 5 = >$100,000 Higher scores indicated a higher annual household income.	1

Table 3.1: Constructs and Operational Definitions Contd.

Construct	Operational definition	Item(s)
Insurance status	One item with six nominal response options was used to measure this construct: Which option best describes the type of health insurance you currently have? 1 = No insurance/Self-pay 2 = Private insurance 3 = Medicare 4 = Medicaid 5 = Not sure 4 = Other (*please specify*) …….	1
Marital status	One item with six nominal response options was used to measure this construct: Which option best describes your marital status? 1= Single, in a relationship 2 = Single, not in a relationship 3 = Married 4 = Partner/Living together 5 = Divorced/Separated 6 = Widowed	1
Stage of breast cancer at diagnosis	One item with six response options was used to measure this construct: At what stage was your breast cancer diagnosed? 1 = Stage 0 2 = Stage 1 3 = Stage 2 4 = Stage 3 5 = Stage 4 6 = Do not know	1
Time since breast cancer diagnosis	One item with four ordinal response options was used to measure this construct: How long ago were you first diagnosed with breast cancer? 1 = 1 year or less 2 = More than 1 year but less than 5 years 3 = More than 5 years but less than 10 years 4 = More than 10 years Higher scores indicated a longer time since breast cancer diagnosis.	1

Table 3.1: Constructs and Operational Definitions Contd.

Construct	Operational definition	Item(s)
Type(s) of breast cancer treatment(s) received	One item with four nominal responses was used to measure this construct: Besides chemotherapy, what other type of breast cancer treatment have you received? *Check all that apply*. 1 = Surgery 2 = Hormone therapy 3 = Radiation therapy 4 = Other (*please specify*) …….	1
Comorbidities	One item with eleven nominal responses was used to measure this construct: In addition to breast cancer, what other illnesses do you have? *Check all that apply*. 1 = Asthma 2 = Arthritis 3 = Diabetes 4 = Hypertension 5 = Hypercholesterolemia 6 = Kidney problems 7 = Heart disease 8 = Anxiety 9 = Depression 10 = Thyroid problems 11 = Other (*please specify*) …….	1

3.4 Sample Size Calculation

Assuming a medium effect size and an alpha of 0.05, and power of 0.80, the sample size needed to conduct the analyses is:

Multiple linear regression

1. Overall model significance

   $N \geq 50 + 8m$

   m = 13 because of the number of independent variables (2) and covariates (11)

   $N \geq 50 + 8\ (13)$

$N \geq 50 + 104$

$N \geq 154$

2. Individual predictors

$N \geq 104 + m$

$m = 13$

$N \geq 104 + 13$

$N \geq 117$

Therefore, a sample size of 154 HER-2 positive breast cancer patients was needed to achieve the study objectives.

3.5 Enrollment and Data Collection

Using continuous enrollment, the clinic's research staff recruited breast cancer patients who met the inclusion/exclusion criteria via convenience sampling, when they showed up for routine clinic visits. Clinic research staff already had human subjects training and those involved in the study were trained on the study protocol prior to patient recruitment. Patients who expressed willingness to participate were assigned a unique study identification number and given the survey cover letter (Appendix 2) and survey instrument by clinic research staff while waiting to see their physician/healthcare provider. The number of patients who were asked but did not consent to participate in the study were also recorded by clinic staff using the informed consent tracking log (Appendix 4).

3.5.1 Inclusion Criteria

The following criteria were applied for study inclusion:

- Adult (age 18 years through 80 years) HER-2 positive breast cancer patients who were receiving chemotherapy/HER2 directed therapy from selected Texas Oncology clinics;
- Patients who had a scheduled office appointment between August and October 2018; and
- Patients who expressed willingness and give their consent to participate.

3.5.2 Exclusion Criteria

Patients with any of the following characteristics were excluded from the study:

- Did not give consent to participate in the study;
- Did not have HER-2 positive breast cancer;
- Was less than 18 years of age or greater than 80 years of age;
- Was not receiving chemotherapy/HER-2 directed therapy;
- Did not have a scheduled office appointment between August and October 2018: and
- Was considered too sick by clinic staff to participate in the study.

IRB procedures

The study was conducted in accordance with the guidelines set forth by The University of Texas Institutional Review Board (IRB). The study application (2017-10-0024) was approved by UT Austin IRB.

3.6 Data Analysis

All data analyses were conducted using SAS 9.4 software. Descriptive statistics were conducted for independent and dependent variables as well as covariates. The *a priori* base alpha level for all inferential analyses to be conducted was set at 0.05, with a power of 0.80. T tests and analysis of variance (ANOVA) were conducted to assess mean differences for independent and dependent variables as well as covariates, while the chi square test/fisher's exact test were used to assess associations between categorical variables. Multiple linear regression was used to predict the effect of the independent variables on the dependent variables, controlling for covariates.

The regression equations are as follows:

$$Y_1 = B_0 + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_4 + B_5X_5 + B_6X_6 + B_7X_7 + B_8X_8 + B_9X_9 + B_{10}X_{10} + B_{11}X_{11} + B_{12}X_{12} + B_{13}X_{13} + B_{14}(X_1X_2) + e_i$$

$$Y_2 = B_0 + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_4 + B_5X_5 + B_6X_6 + B_7X_7 + B_8X_8 + B_9X_9 + B_{10}X_{10} + B_{11}X_{11} + B_{12}X_{12} + B_{13}X_{13} + B_{14}(X_1X_2) + e_i$$

$$Y_3 = B_0 + B_1X_1 + B_2X_2 + B_3X_3 + B_4X_4 + B_5X_5 + B_6X_6 + B_7X_7 + B_8X_8 + B_9X_9 + B_{10}X_{10} + B_{11}X_{11} + B_{12}X_{12} + B_{13}X_{13} + B_{14}(X_1X_2) + e_i$$

Y_1= Cancer health related quality of life

Y_2 = Number of cancer-related emergency department visits

Y_3 = Number of cancer-related hospitalizations

B_0 = Intercept

X_1 = Cancer health literacy

X_2 = Patient activation

X_3 = Age

X_4 = Gender

X_5 = Educational level

X_6 = Ethnicity

X_7 = Household income

X_8 = Insurance status

X_9 = Marital status

X_{10} = Stage of breast cancer at diagnosis

X_{11} = Time since diagnosis

X_{12} = Type of breast cancer treatment received

X_{13} = Comorbidities

e_i = Error term

B1-14 are the regression coefficients for the respective predictor variables.

Statistical Assumptions

The multiple regression assumptions of normality, linearity, and homoscedasticity were tested for continuous and interval-level variables before running further analysis. Normality was assessed by examining the peakedness (kurtosis) and symmetry (skewness) of the distribution. Skewness refers to the degree to which a distribution is asymmetric while kurtosis addresses the degree to which a distribution deviates from the "peakedness" of a distribution. These were assessed using frequency histograms, residual scatterplots, probability plots, and statistical results provided via proc univariate. Skewness and kurtosis values greater than |2| and |7|, respectively, are a cause of concern for multivariate data.[147,148]

The assumption of linearity is that a straight-line relationship exists between independent and dependent variables. This assumption was evaluated by assessing bivariate scatterplots of each interval-level independent variable and dependent variable.

A visual examination of the scatterplots was also performed to test the assumption that the variance of error was equal across all levels of the independent variables (homoscedasticity). Violations of the linearity and homoscedasticity assumptions do not compromise data analyses, but rather weakens them. Variable transformation may be warranted in cases of serious heteroscedasticity which occurs when the spread in standard deviations of residuals around predicted values is three times higher for the widest spread as for the most narrow spread.[147] ANOVA and independent groups t-test have similar normality, linearity, and homoscedasticity assumptions.

Multicollinearity is an additional problem often encountered in multiple regression analysis. It occurs when two predictor variables are highly correlated with one another, which if left undetected can prevent a predictor variable from reaching its statistical significance. Multicollinearity between independent variables was assessed in order to determine whether predictors were correlated among themselves. Presence of multicollinearity could greatly affect the results of a study by inflating the standard deviation of a regression weight and decreasing power. A rule of thumb to detect multicollinearity is a tolerance of less than 0.10 or a variance inflation factor (1 divided by tolerance) greater than 10 where tolerance = $1 - R^2$. R^2 represents the proportion of variance in the first variable shared with the second variable. If significant collinearity exists between variables, only one variable is utilized in the regression analyses.[147]

The chi square test assumptions of independence and percentage of expected cell counts were also assessed prior to running any analysis. Fisher's exact test was used in instances where more than 20 percent of the expected cell counts were less than five.[149] Table 3.2 contains the measurement level for each variable, while table 3.3 contains a summary of the study objectives, hypotheses, and corresponding statistical tests.

Table 3.2: Study Variables, Measurement Level, and Statistical Tests

Study variable	Measurement level	Statistical test
Independent variable		
Cancer health literacy level	Ordinal	
General health literacy level	Ordinal	
Patient activation score	Interval	
Patient activation level	Ordinal	
Dependent variables		
Cancer health-related quality of life	Interval	
Number of cancer-related emergency department visits	Interval	
Number of cancer-related hospitalizations	Interval	**Descriptive Statistics** • Mean, standard deviation (SD), median, mode, skewness, and kurtosis for continuous/interval variables • Frequencies for ordinal and nominal variables
Quality of patient-provider communication	Interval	
Covariates		
Age	Interval	
Gender	Nominal	
Educational level	Ordinal	
Ethnicity	Nominal	
Household income	Ordinal	
Insurance status	Nominal	
Marital status	Nominal	
Stage of breast cancer at diagnosis	Ordinal	
Time since diagnosis	Ordinal	
Type of breast cancer treatment received	Nominal	
Comorbidities	Nominal	

Table 3.3: Study Objectives, Hypotheses, and Corresponding Statistical Tests

Objectives/Hypotheses	Dependent Variables	Independent Variables	Statistical Test
Objective 1: To describe cancer health literacy, patient activation, clinical (stage of breast cancer at diagnosis, time since diagnosis, type of breast cancer treatment received, comorbidities) and demographic (age, gender, educational level, ethnicity, household income, insurance status, marital status) characteristics of a of breast cancer patient sample.			Mean, Standard deviation (SD), Frequency
Objective 2: To examine the relationship between health literacy and clinical and demographic characteristics in a sample of breast cancer patients.			
	Cancer health literacy General health literacy	Age	T-test
		Gender	Chi-square test
		Educational level	
		Ethnicity	
		Household income	
		Insurance status	
		Marital status	
		Stage of breast cancer at diagnosis	
		Time since diagnosis	
		Type of breast cancer treatment received	
		Comorbidities	
Objective 3: To examine the relationship between patient activation and clinical and demographic characteristics in a sample of breast cancer patients.			
	Patient activation	Age	Correlation
		Gender	ANOVA
		Educational level	
		Ethnicity	
		Household income	
		Insurance status	
		Marital status	
		Stage of breast cancer at diagnosis	

Table 3.3: Study Objectives, Hypotheses, and Corresponding Statistical Tests Contd.

		Time since diagnosis	
		Type of breast cancer treatment received	
		Comorbidities	
Objective 4: To assess the relationship between cancer health literacy and patient activation in a sample of breast cancer patients.			
H1: Breast cancer patients who have adequate cancer health literacy will have higher patient activation compared to those that have limited cancer health literacy.	Cancer health literacy	Patient activation	T-test
Objective 5: To examine the relationship between cancer health literacy and patient-provider communication in a sample of breast cancer patients.			
H2: Breast cancer patients who have adequate cancer health literacy will have easier patient-provider communication and understanding of information provided compared to those that have limited cancer health literacy.	Cancer health literacy	Quality of patient-provider communication	T test
Objective 6: To examine the relationship between cancer health literacy and general health literacy in a sample of breast cancer patients.			
H3: There will be a significant positive relationship between cancer health literacy and general health literacy in the sample of breast cancer patient	Cancer health literacy	General health literacy	Chi-square test
Objective 7: To determine the overall predictive validity of the health literacy skills (HLS) framework in explaining health outcomes (cancer health-related quality of life, cancer-related emergency department visits, and cancer-related hospitalizations) using cancer health literacy and patient activation, controlling for cancer health literacy X patient activation interaction and clinical/demographic characteristics.			

Table 3.3: Study Objectives, Hypotheses, and Corresponding Statistical Tests Contd.

H4: Cancer health literacy and patient activation will explain a significant amount of variance in cancer health-related quality of life controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics	Cancer HRQoL	Cancer health literacy Patient activation Clinical and demo-graphic covariates	Multiple linear regression: R^2; F test
H5: Cancer health literacy and patient activation will explain a significant amount of variance in cancer-related emergency department visits controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics	Number of cancer-related emergency department visits		
H6: Cancer health literacy and patient activation will explain a significant amount of variance in cancer-related hospitalizations controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics	Number of cancer-related hospitalizations		
Objective 8: To predict health-related quality of life in breast cancer patients using cancer health literacy and patient activation controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic characteristics			
H7: Cancer health literacy and patient activation will be significant positive predictors of cancer health-related quality of life controlling for	Cancer HRQoL	Cancer health literacy Patient activation	Multiple linear regression: R^2; F test

Table 3.3: Study Objectives, Hypotheses, and Corresponding Statistical Tests Contd.

the interaction between cancer health literacy and patient activation as well as clinical and demographic variables.		Clinical and demographic covariates	
Objective 9: To predict cancer-related emergency department visits in breast cancer patients using cancer health literacy and patient activation controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic variables.			
H8: Cancer health literacy and patient activation will be significant negative predictors of cancer-related emergency department visits controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic variables.	Number of cancer-related emergency department visits	Cancer health literacy Patient activation Clinical and demographic covariates	Multiple linear regression: R^2; F test
Objective 10: To predict cancer-related hospitalizations in breast cancer patients using cancer health literacy and patient activation controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic variables.			
H9: Cancer health literacy and patient activation will be significant negative predictors of cancer-related hospitalizations controlling for the interaction between cancer health literacy and patient activation as well as clinical and demographic variables.	Number of cancer-related hospitalizations	Cancer health literacy Patient activation Clinical and demographic covariates	Multiple linear regression: R^2; F test

3.7 Study Timeline

The study was conducted over a period of seven months. Patients were continuously enrolled from August to October 2018. Patients were asked to fill out the survey while waiting to see the physician/healthcare provider during office visits. Analysis of the survey responses were conducted after the target number of patients had completed the survey. Table 3.4 contains the details of the study timeline.

Table 3.4: Study Timeline

Activity name	Start date	End date	Duration	Aug 2018	Sept 2018	Oct 2018	Nov 2018	Dec 2018	Jan 2019	Feb 2019
Project duration	08/18	2/18	7 months							
Obtain consent and administer survey	08/18	10/18	3 months							
Data analysis and write-up	11/18	2/19	4 months							

Chapter 4: Results

The main findings of the study are discussed in this chapter. First, results from the pretest form are discussed followed by details of the data preparation process and preliminary data analysis results. Next, the demographics of study participants are described. Finally, the results of bivariate and multivariate analyses conducted to test study hypotheses are presented in detail.

4.1 Pretest Results

Three breast cancer patients who met the study's inclusion/exclusion criteria evaluated the study survey upon completion using a survey evaluation form (Appendix 5). The evaluation form consisted of questions to assess the survey based on the readability of survey items, relevance of survey items, survey format, and time required to complete the survey.

The three respondents completed the survey within 10 minutes. With regards to readability, the three patients stated that all survey items were clear and easy to understand. They also concurred that all survey items were relevant to the research and two agreed that there were no missing issues of importance. However, one patient suggested that questions regarding diet should have been included in the study stating that "what you eat is very important…when fighting cancer or inflammation." Finally, all three patients found the survey format user friendly and easy to follow.

4.2 Data Preparation and Cleaning

One hundred and sixty-four patients who met the study's inclusion/exclusion criteria were approached by clinical staff in 12 Texas Oncology clinics and offered participation in the study. The response rate was high (90%) as 147 patients gave their consent to participate and completed the survey. However, the responses of one patient were excluded because she had not yet begun treatment, leading to a final study sample size of 146. Table 4.1 and Figure 4.1 contain details of study participation by clinic.

Table 4.1 Study Participation by Clinic

S/N	Site Name	Completed	Declined	Total
1	Austin Central	4	1	5
2	Austin Midtown	7	0	7
3	Austin Round Rock	15	3	18
4	Austin South	3	2	5
5	Dallas Presbyterian	34	0	34
6	El Paso Grandview	5	0	5
7	Mesquite	11*	0	11
8	Rockwall	15	0	15
9	San Antonio Downtown	5	6	11
10	San Antonio NE	16	3	19
11	San Antonio SO	10	0	10
12	Tyler	22	2	24
		147	**17**	**164**

*patient responses were excluded from study because patient did not meet inclusion/exclusion criteria

= Cities where participating clinics were located
https://www.worldatlas.com/webimage/countrys/namerica/usstates/cities/txmjcity.htm

Figure 4.1 Map of Texas Showing Location of Participating Clinics

Responses to the 6 items on the cancer health literacy tool (CHLT-6) were used to generate probabilities of adequate and limited cancer health literacy using the CHLT-6 algorithm. The responses of patients to the 6 items of the Newest Vital Scale were scored as right (1) or wrong (0) and summed up. Patients were considered to either have limited general health literacy (total score less than 4) or adequate literacy (total score 4 to 6) based on their total NVS score. The responses of patients to the 13 items of the Patient Activation Measure (PAM-13) were also converted to a PAM score on the 0 – 100 scale, using the PAM-13 score spreadsheet. The generated health literacy and PAM scores were then used in subsequent analyses.

For the covariates, gender was excluded from bivariate and multivariate analysis because 99.3 percent of the study sample was female. The education variable was dichotomized into low formal education (patients with less than high school education and high school graduate/GED) and high formal education (patients with college and post graduate degrees). Also, a majority of patients received multiple types of treatment and had multiple comorbidities so patient responses to these items were summed up to get a composite score for the number of treatment types received as well as the number of comorbidities, respectively. The responses of the study participants were compiled in a single Excel spreadsheet that was subsequently uploaded into SAS 9.4 (SAS Institute, Cary, N.C.) for data preparation, screening, and analysis. Data were then assessed for normality, outliers and extent of missing data.

4.3 Preliminary Data Analysis

The normality of interval level variables was assessed by measuring the symmetry and kurtosis of each variable's distribution. None of the interval level variables were problematic as their values fell within the threshold for skewness (|2|) and kurtosis (|7|). See Table 4.2. Potential outliers were screened for by inspecting z-scores of continuous, interval variables. No outliers were identified in the data. Thirty-one instances of missing data were observed across nine demographic/clinical survey items and the two communication items. One patient had no entry for the number of ED visits and hospitalizations items. Patients were not required to have a comorbidity so blank entries for this item were not considered missing data. For the CHLT-6, NVS, PAM-13, and FACT-G items, recommended techniques were employed to generate scores for partially completed scale items.[18,133,139,145,146] For FACT-G missing items, subscale scores were prorated by multiplying the sum of the subscale by the number of items in the subscale,

then dividing by the number of items actually answered. For PAM scores missing items were designated N/A and for the health literacy items (CHLT-6 and NVS), unanswered questions were scored as 0. Two individuals had no entries at all for the Newest Vital Sign items.

Table 4.2 Skewness and Kurtosis Values of Interval Level Variables

Variable	Skewness	Kurtosis
Age	-0.13	-0.64
PAM scores	0.53	-0.45
Patient communicating breast cancer concerns to health care provider	-1.91	3.05
Patient understanding of information given by healthcare providers	-0.96	0.28
Number of treatment types received	-0.17	-0.79
Number of comorbidities	1.05	0.63

Furthermore, the assumptions of normality, homoscedasticity, linearity, independence, and multicollinearity of the quality of life dependent variable (overall FACT-G score) were checked prior to multivariate statistical analyses. The distributions of the residuals were found to be normal based on histograms of the residuals and normal probability plots. The assumption of homoscedasticity was also assessed by examining a scatterplot of the residuals against the predicted values. Even though there was some heteroscedasticity, Ordinary Least Square (OLS) regression is robust to minor violations of this assumption. Based on the non-curved shape of the residual scatter plots, the assumption of linearity of residuals was met. Since participants responded individually to the survey, the assumption of independence was met. Finally, multicollinearity was tested by performing collinearity diagnostics and assessing the tolerance and variance inflation

factor between each pair of independent variables. None of the tolerance values were less than 0.1, and none of the variation factors were greater than 10. Therefore, multicollinearity was not considered a problem and all demographic/clinical variables were eligible to be used in the multiple regression analysis.

After checking for multicollinearity and violations of assumptions, no rescoring or transformation of the data was deemed necessary. The quality of life variable did not have violations of skewness and kurtosis, and its distribution was approximately normal. Upon completion of preliminary data analysis, descriptive, bivariate and multivariate analyses were conducted to achieve the study objectives and test study hypotheses. These analyses and their results are outlined in detail below.

4.4 Descriptive Statistics Results

The demographic and clinical characteristics of the study participants are described in this section and details are listed in Table 4.3. The average age of study participants was 57.1±10.8 years. The majority were female (99.3%), Caucasian (71.7%), married or in a relationship (69.5%), had a high formal education level (52.8%), had private insurance (59.7%), and had an annual household income over $50,000 (66.2%). Clinically, patients were widely distributed across the four stages of breast cancer (stage 1 to stage 4), and most patients had been diagnosed for the first time within the last 5 years (78.0%). The majority (79.4%) of patients had two comorbidities or less with hypertension (27.6%) being the most common comorbidity.

Table 4.3 Demographic and Clinical Characteristics of Study Participants

Variable	Mean (SD)
Age (n = 141)	57.1 (10.8)
	Frequency (%)*
Gender (n = 145)	
Male	1 (0.7)
Female	144 (99.3)
Race (n = 145)	
African-American or non-Hispanic black	12 (8.3)
Asian-American or Pacific Islander	5 (3.5)
Caucasian or non-Hispanic white	104 (71.7)
Mexican-American or Hispanic	18 (12.4)
Other†	6 (4.1)
Educational level (n = 144)	
Low formal education	68 (47.2)
High formal education	76 (52.8)
Household income (n = 136)	
Less than $25,000	24 (17.6)
$25,000 to $50,000	22 (16.2)
> $50,000 to $75,000	33 (24.3)
> $75,000 to $100,000	25 (18.4)
> $100,000	32 (23.5)
Insurance status (n = 144)	
Private insurance	86 (59.7)
Medicare	21 (14.6)
Medicaid	15 (10.4)
Multiple	21 (14.6)
Other†	1 (0.7)

Table 4.3 Demographic and Clinical Characteristics of Study Participants Contd.

Marital status (n = 144)	
Single, in a relationship	7 (4.9)
Single, not in a relationship	17 (11.8)
Married	87 (60.4)
Partner/Living together	6 (4.2)
Divorced/Separated	18 (12.5)
Widowed	9 (6.2)
Stage of breast cancer at diagnosis (n = 144)	
Stage 0	4 (2.8)
Stage 1	33 (22.9)
Stage 2	32 (22.2)
Stage 3	32 (22.2)
Stage 4	35 (24.3)
Do not know	8 (5.6)
Time since breast cancer diagnosis (n = 144)	
1 year or less	73 (50.4)
More than 1 year but less than 5 years	40 (27.6)
More than 5 years but less than 10 years	17 (11.7)
More than 10 years	15 (10.3)
Number of breast cancer treatment types received (n = 146)	
1	22 (15.1)
2	31 (21.2)
3	51 (34.9)
4	37 (25.4)
5	5 (3.4)
Type of breast cancer treatment received (n = 146)	
Chemotherapy alone	22 (15.1)
Chemotherapy + Radiation	2 (1.4)
Chemotherapy + Surgery	21 (14.4)

Table 4.3 Demographic and Clinical Characteristics of Study Participants Contd.

Chemotherapy + Hormone	7 (4.8)
Chemotherapy + Herceptin	1 (0.7)
Multiple	93 (63.7)
Number of comorbidities (n = 146)	
0	39 (26.7)
1	42 (28.8)
2	34 (23.3)
3	17 (11.6)
4	10 (6.8)
5	3 (2.1)
6	1 (0.7)
Comorbidity type (n = 146)*	
Hypertension	40 (27.6)
High cholesterol	29 (20.0)
Arthritis	26 (17.9)
Depression	25 (17.2)
Thyroid problems	25 (17.2)
Anxiety	24 (16.6)
Diabetes	19 (13.1)
Asthma	13 (9.0)
Heart disease	6 (4.1)
Kidney problems	2 (1.4)
Osteoporosis	2 (1.4)
Other†	9 (6.2)

*Sum of percentage values is not equal to 100% because some patients reported multiple categories or none
†"Other" category for insurance and comorbidity type was not specified; For race, "other" category consisted of mixed race or not specified.

For the independent variables, 92 percent (N=134) of participants had adequate cancer health literacy while 79 percent (N=114) had adequate general health literacy based on their CHLT-6 and NVS scores, respectively. The reliability of the general health literacy instrument (NVS) was evaluated using Cronbach's coefficient alpha. The NVS had moderate internal consistency (alpha=0.67). The mean patient activation score was 65.9±15.7 (range 34.2 to 100.0) with most patients (68%, N=99) in the higher levels (level 3 or 4) of activation (Table 4.4). The Cronbach's coefficient alpha of the PAM was 0.88 which indicated a high internal consistency.

Table 4.4 Patient Activation Level Distribution (N=146)

Patient activation level (n = 146)	Frequency (%)
Level 1	16 (11.0)
Level 2	31 (21.2)
Level 3	46 (31.5)
Level 4	53 (36.3)

With regards to the dependent variables, the average quality of life based on FACT-G scores was 82.6±16.1 (range 36.0 to 108.0) with emotional well-being having the highest domain average (19.6 out of 24.0)) and functional well-being having the lowest domain average (20.1 out of 28.0) (Table 4.5). The Cronbach's coefficient alpha of the overall FACT-G score was 0.92 which indicated a high internal consistency. The internal consistency was also generally high for the four FACT-G domains.

Table 4.5 FACT-G Scores

FACT-G domain	Mean (SD)	Range	Reliability
Physical well-being	20.3 (6.2)	2.0 - 28.0	0.89
Social well-being	22.6 (5.3)	2.0 - 28.0	0.88
Emotional well-being	19.6 (3.4)	8.4 - 24.0	0.68
Functional well-being	20.1 (5.7)	4.0 - 28.0	0.85
Overall FACT-G	**82.6 (16.1)**	**36.0 - 108.0**	**0.92**

The majority of patients found it somewhat or extremely easy (90.2%, N= 128) to communicate their breast cancer concerns to their healthcare provider and somewhat or extremely easy (83.5%, N= 121) to understand information given by healthcare providers about breast cancer and its management (Table 4.6).

Only five patients (3.4%) reported an ED visit and two patients (1.4%) reported a hospitalization in the last 30 days due to a breast cancer complication.

Table 4.6 Communication Difficulty Frequency Distribution and Means

Communication Difficulty	Frequency (%)					Mean (SD)
	Extremely difficult	Somewhat difficult	Neither easy nor difficult	Somewhat easy	Extremely easy	
Difficulty of communicating breast cancer concerns to healthcare provider (N=142)	0 (0.0)	4 (2.8)	10 (7.0)	25 (17.6)	103 (72.6)	4.6 (0.7)
Difficulty of understanding information given by healthcare providers about breast cancer and its management (N=145)	0 (0.0)	6 (4.1)	18 (12.4)	53 (36.6)	68 (46.9)	4.3 (0.8)

4.5 Bivariate Analysis Results

Bivariate data analyses were conducted using t-tests, correlations, ANOVA, and fisher's exact tests to assess relationships between variables and test study hypotheses as outlined below:

4.5.1 To examine the relationships between cancer health literacy and clinical/demographic characteristics in a sample of breast cancer patients. Ninety-two percent of study participants (N=134) had adequate cancer health literacy while eight percent (N=12) had limited cancer health literacy.

Results in Table 4.7 show that there were no significant relationships between cancer health literacy and most clinical/demographic variables except for household income (X^2=12.84; df=4; p=0.0198) and education (X^2=6.85; df=1; 0.0132). Most patients with adequate

cancer health literacy earned over $50,000 (68.0%, N= 85) and were highly educated (at least had a college degree), while many patients with limited cancer health literacy earned less than $25,000 (54.5%, N= 6) and had low formal education (had high school education/GED or less).

Table 4.7 Relationships between Cancer Health Literacy and Clinical/Demographic Variables

Variable	**Limited Cancer Health Literacy**	**Adequate Cancer Health Literacy**	**T test**	**p value**
	N Mean (SD)			
Age	11 57.2 (10.0)	130 57.1 (10.9)	0.04	0.9702
Number of comorbidities	12 1.6 (1.8)	134 1.5 (1.3)	0.17	0.8672
Number of treatments received	12 2.6 (1.0)	134 2.8 (1.1)	0.75	0.4554
	Frequency (%)		X^2	**p value**
Race (n = 145)				
African-American or non-Hispanic black	2 (16.7)	10 (7.5)	7.58	0.1122
Asian-American or Pacific Islander	0 (0.0)	5 (3.8)		
Caucasian or non-Hispanic white	6 (50.0)	98 (73.7)		
Mexican-American or Hispanic	4 (33.3)	14 (10.5)		
Other	0 (0.0)	6 (4.5)		
Educational level (n = 144)				
Low formal education	10 (83.3)	58 (43.9)	6.85	**0.0132**
High formal education	2 (16.7)	74 (56.1)		

Table 4.7 Relationships between Cancer Health Literacy and Clinical/Demographic Variables Contd.

Household income (n = 136)				
Less than $25,000	6 (54.5)	18 (14.4)	12.84	**0.0198**
$25,000 to $50,000	0 (0.0)	22 (17.6)		
> $50,000 to $75,000	3 (27.3)	30 (24.0)		
> $75,000 to $100,000	1 (9.1)	24 (19.2)		
> $100,000	1 (9.1)	31 (24.8)		
Insurance status (n = 144)				
Private insurance	5 (41.7)	81 (61.4)	4.80	0.2067
Medicare	3(25.0)	18 (13.6)		
Medicaid	3 (25.0)	12 (9.1)		
Multiple	1 (8.3)	20 (15.1)		
Other	0 (0.0)	1 (0.8)		
Marital status (n = 144)				
Single, in a relationship	0 (0.0)	7 (5.3)	8.32	0.0871
Single, not in a relationship	3 (27.3)	14 (10.5)		
Married	5 (45.4)	82 (61.6)		
Partner/Living together	1 (9.1)	5 (3.8)		
Divorced/Separated	0 (0.0)	18 (13.5)		
Widowed	2 (18.2)	7 (5.3)		
Stage of breast cancer at diagnosis (n = 144)				
Stage 0	1 (8.3)	3 (2.3)	5.81	0.2476
Stage 1	1 (8.3)	32 (24.2)		
Stage 2	2 (16.7)	30 (22.7)		
Stage 3	3 (25.0)	29 (22.0)		
Stage 4	3 (25.0)	32 (24.2)		
Do not know	2 (16.7)	6 (4.6)		

Table 4.7 Relationships between Cancer Health Literacy and Clinical/Demographic Variables Contd.

Time since breast cancer diagnosis (n = 145)				
1 year or less	5 (41.7)	68 (51.1)	2.76	0.4580
More than 1 year but less than 5 years	5 (41.7)	35 (26.3)		
More than 5 years but less than 10 years	2 (16.6)	15 (11.3)		
More than 10 years	0 (0.0)	15 (11.3)		

T-tests conducted for interval variables (age, number of comorbidities, number of treatment types received). Fisher's exact test conducted for other variables.

4.5.2 To examine the relationships between general health literacy and clinical/demographic characteristics in a sample of breast cancer patients. Seventy-nine percent of study participants (N=114) had adequate general health literacy while twenty-one percent had limited general health literacy (N=30).

Results in Table 4.8 show that there were no significant relationships between general health literacy and most clinical/demographic variables except for age (t=2.28; df=137; p=0.0244), education (X^2=4.14; df=1; p=0.0419) and insurance (X^2=9.3; df=4; p=0.0441). Patients with adequate general health literacy were significantly younger (56.0±10.8 years) than patients with limited general health literacy (61.2±9.9 years). Patients with adequate general health literacy also tended to have a high level of formal educational (57.5%, N=65) while those with limited general health literacy tended to have low formal education (63.3%, N= 19). In addition, more than half of patients with adequate general health literacy had private insurance alone (65.2%, N= 73), while a third of patients with limited general health literacy had Medicare or Medicaid only (33.3%, N=10).

Table 4.8 Relationships between General Health Literacy and Clinical/Demographic Variables

Variable	Limited General Health Literacy	Adequate General Health Literacy	T test	p value
	N Mean (SD)			
Age	27 61.1 (9.7)	112 56.0 (10.8)	2.28	**0.0244**
Number of comorbidities	30 1.5 (1.6)	114 1.5 (1.3)	0.03	0.9747
Number of treatments received	30 2.6 (0.9)	114 2.9 (1.1)	1.32	0.1902
	Frequency (%)		X^2	**p value**
Race (n = 143)				
African-American or non-Hispanic black	5 (16.7)	7 (6.2)	4.48	0.2578
Asian-American or Pacific Islander	1 (3.3)	4 (3.5)		
Caucasian or non-Hispanic white	18 (60.0)	85 (75.2)		
Mexican-American or Hispanic	4 (13.3)	13 (11.5)		
Other	2 (6.7)	4 (3.6)		
Educational level (n = 143)				
Low formal education	19 (63.3)	48 (42.5)	4.14	**0.0419**
High formal education	11 (36.7)	65 (57.5)		
Household income (n = 134)				
Less than $25,000	7 (28.0)	17 (15.6)	2.54	0.6675
$25,000 to $50,000	4 (16.0)	18 (16.5)		
> $50,000 to $75,000	6 (24.0)	26 (23.8)		
> $75,000 to $100,000	4 (16.0)	21 (19.3)		
> $100,000	4 (16.0)	27 (24.8)		

Table 4.8 Relationships between General Health Literacy and Clinical/Demographic Variables Contd.

Insurance status (n = 142)				
Private insurance	12 (40.0)	73 (65.2)	9.34	**0.0441**
Medicare	6 (20.0)	14 (12.5)		
Medicaid	4 (13.3)	11 (9.8)		
Multiple	7 (23.4)	14 (12.5)		
Other	1 (3.3)	0 (0.0)		
Marital status (n = 142)				
Single, in a relationship	1 (3.5)	6 (5.3)	4.19	0.4460
Single, not in a relationship	5 (17.2)	12 (10.6)		
Married	16 (55.2)	70 (62.0)		
Partner/Living together	2 (6.9)	4 (3.5)		
Divorced/Separated	2 (6.9)	16 (14.2)		
Widowed	3 (10.3)	5 (4.4)		
Stage of breast cancer at diagnosis (n = 142)				
Stage 0	1 (3.3)	3 (2.7)	9.55	0.1220
Stage 1	5 (16.7)	28 (25.0)		
Stage 2	5 (16.7)	26 (23.2)		
Stage 3	6 (20.00)	25 (22.3)		
Stage 4	8 (26.6)	27 (24.1)		
Do not know	5 (16.7)	3 (2.7)		
Time since breast cancer diagnosis (n = 143)				
1 year or less	12 (40.0)	60 (53.1)	2.06	0.5322
More than 1 year but less than 5 years	10 (33.3)	29 (25.7)		
More than 5 years but less than 10 years	5 (16.7)	12 (10.6)		
More than 10 years	3 (10.0)	12 (10.6)		

T-tests conducted for interval variables (age, number of comorbidities, number of treatment types received). Chi-square test conducted for education variable. Fisher's exact test conducted for other variables.

4.5.3 To examine the relationships between patient activation score and clinical/demographic characteristics in a sample of breast cancer patients. The mean patient activation score was 65.9±15.7 (range 34.2 to 100.0) with most patients (68%, N=99) in the higher levels (level 3 or 4) of activation

Results in Table 4.9 showed no statistically significant differences in patient activation scores across most clinical/demographic variables except for race. A Tukey's post-hoc test showed that the mean patient activation score for Caucasians (68.9±16.0) was significantly higher than that for Blacks (54.5±6.9) and Hispanics (58.3±10.7) at an alpha level of $p < 0.05$.

Table 4.9 Relationships between Patient Activation and Clinical/Demographic Variables

Variable	**Correlation**		**p value**
Age (n=141)	0.11		0.1872
Number of comorbidities (n=146)	0.06		0.4644
Number of treatments received (n=146)	0.06		0.4727
	Mean Patient Activation Score (SD)	**F value**	**p value**
Race (n = 145)			
African-American or non-Hispanic black	54.5 (6.9)	4.01	**0.0041**
Asian-American or Pacific Islander	62.2 (23.4)		
Caucasian or non-Hispanic white	68.9 (16.1)		
Mexican-American or Hispanic	58.3 (10.7)		
Other	65.0 (10.0)		
Educational level (n = 144)			
Low formal education	64.3 (15.9)	1.24	0.2683
High formal education	67.2 (15.3)		

Table 4.9 Relationships between Patient Activation and Clinical/Demographic Variables Contd.

Household income (n = 136)			
Less than $25,000	63.9 (15.8)	0.56	0.6915
$25,000 to $50,000	66.2 (16.9)		
> $50,000 to $75,000	68.3 (15.8)		
> $75,000 to $100,000	63.8 (16.4)		
> $100,000	68.5 (14.9)		
Insurance status (n = 144)			
Private insurance	66.2 (16.0)	0.20	0.8966
Medicare	67.1 (18.1)		
Medicaid	64.1 (11.1)		
Multiple	64.7 (15.6)		
Other	58.1 (0.00)		
Marital status (n = 144)			
Single, in a relationship	65.5 (18.5)	1.74	0.1668
Single, not in a relationship	62.8 (12.5)		
Married	67.0 (16.6)		
Partner/Living together	68.0 (13.1)		
Divorced/Separated	60.2 (13.5)		
Widowed	75.0 (12.2)		
Stage of breast cancer at diagnosis (n = 144)			
Stage 0	55.4 (10.2)	2.27	0.0797
Stage 1	65.9 (15.2)		
Stage 2	66.7 (15.3)		
Stage 3	65.6 (17.1)		
Stage 4	69.0 (16.6)		
Do not know	57.0 (8.9)		

Table 4.9 Relationships between Patient Activation and Clinical/Demographic Variables Contd.

Time since breast cancer diagnosis (n = 145)			
1 year or less	65.6 (15.0)	0.16	0.9212
More than 1 year but less than 5 years	66.4 (14.5)		
More than 5 years but less than 10 years	68.5 (19.0)		
More than 10 years	64.3 (18.8)		

Pearson's correlation conducted for interval variables (age, number of comorbidities, number of treatment types received). ANOVA conducted for other variables.

4.5.4 To assess the relationship between cancer health literacy and patient activation in a sample of breast cancer patients.

H1: Breast cancer patients who have adequate cancer health literacy will have a higher patient activation score compared to those that have limited cancer health literacy.

An independent groups t-test showed no significant difference in mean patient activation score between patients with limited cancer health literacy (63.7±10.4) and those with adequate cancer health literacy (66.1±16.1) (t=0.50; df=144; p=0.62). Therefore, hypothesis H1 was not supported.

4.5.4 To examine the relationship between cancer health literacy and patient-provider communication in a sample of breast cancer patients.

H2: Breast cancer patients who have adequate cancer health literacy will have easier patient-provider communication and understanding of information provided compared to those that have limited cancer health literacy.

An independent groups t-test showed no significant difference in the ease of communicating breast cancer concerns to a healthcare provider between patients with

limited cancer health literacy (4.5±0.7) and patients with adequate cancer health literacy (4.6±0.7) (t=0.43; df=140; p=0.67). Also, there was no significant difference in the ease of understanding information given by healthcare providers about breast cancer and its management between patients with limited cancer health literacy (3.7±1.2) and patients with adequate cancer health literacy (4.3±0.8) (t =1.91; df =11.9; p=0.08). Therefore, hypothesis H2 was not supported in terms of communication and understanding. Tables 4.10 and 4.11 show the distribution of patient responses to the communication and understanding items by cancer health literacy level.

Table 4.10 Relationship between Communicating Breast Cancer Concerns to Healthcare Provider and Cancer Health Literacy Level (N=142)

Difficulty of communicating breast cancer concerns to healthcare provider	Frequency (%)					Mean (SD)	T test	p value
	Extremely difficult	Somewhat difficult	Neither easy nor difficult	Somewhat easy	Extremely easy			
Limited cancer health literacy	0 (0.0)	0 (0.0)	1 (10.0)	3 (30.0)	6 (60.0)	4.5 (0.7)	0.43	0. 6655
Adequate cancer health literacy	0 (0.0)	4 (3.0)	9 (6.8)	22 (16.7)	97 (73.5)	4.6 (0.7)		

Table 4.11 Relationship between Patient Understanding of Information given by Healthcare Providers on Breast Cancer and Cancer Health Literacy Level (N=145)

Difficulty of understanding information given by healthcare providers about breast cancer and its management	Frequency (%)					Mean (SD)	T test	p value
	Extremely difficult	Somewhat difficult	Neither easy nor difficult	Somewhat easy	Extremely easy			
Limited cancer health literacy	0 (0.0)	2 (16.7)	4 (33.3)	2 (16.7)	4 (33.3)	3.7 (1.2)	1.91	0.0807
Adequate cancer health literacy	0 (0.0)	4 (3.0)	14 (10.5)	51 (38.4)	64 (48.1)	4.3 (0.8)		

4.5.5 To assess the relationship between cancer health literacy and general health literacy in a sample of breast cancer patients.

H3: There will be a positive relationship between cancer health literacy and general health literacy in the sample of breast cancer patients.

A Chi square analysis revealed a significant relationship between cancer health literacy and general health literacy (X^2= 8.21; df = 1; p = 0.0042). Most patients who had adequate cancer health literacy (82.0%, N=109) also had adequate general health literacy. See Table 4.12. Therefore, hypothesis H3 was supported.

Table 4.12 Cancer Health Literacy vs General Health Literacy (N=144)

Variable	Frequency (%)		X^2	p value
	Limited Cancer Health Literacy	Adequate Cancer Health Literacy		
Limited General Health Literacy	6 (54.5)	24 (18.0)	8.21	**0.0109**
Adequate General Health Literacy	5 (45.5)	109 (82.0)		

4.6 Multivariate Analysis Results

Multivariate data analyses were conducted using linear regression to assess relationships between variables and test other study hypotheses. Due to the low number of cancer-related ED visits (3.4%, N=5) and hospitalizations (1.4%, N=2) reported by study participants, multivariate analyses were not conducted on these two dependent variables.

Bivariate analyses were completed on the quality of life dependent variable (overall FACT-G score) and independent variables to develop a parsimonious model (Table 4.13). All clinical/demographic factors that were not related to the quality of life dependent variable were excluded from the multivariate analyses. Eight of the ten clinical/demographic variables were dropped. The retained clinical/demographic factors were education and number of treatment types received.

Table 4.13 Relationships between Health-Related Quality of Life (Overall FACT-G Score) and Clinical/Demographic Variables

Variable	Correlation		p value
Age (n=141)	0.10		0.2236
Number of comorbidities (n=146)	0.13		0.1157
Number of treatment types received (n= 146)	0.21		**0.0101**
	Mean FACT-G Score (SD)	**F value**	**p value**
Race (n = 145)			
African-American or non-Hispanic black	76.0 (13.9)	2.29	0.1048
Asian-American or Pacific Islander	70.6 (12.3)		
Caucasian or non-Hispanic white	84.8 (16.0)		
Mexican-American or Hispanic	78.7 (18.7)		
Other	80.7 (9.0)		
Educational level (n = 144)			
Low formal education	79.2 (17.7)	5.97	**0.0158**
High formal education	85.7 (14.1)		
Household income (n = 136)			
Less than $25,000	78.3 (16.1)	0.74	0.5656
$25,000 to $50,000	83.6 (16.4)		
> $50,000 to $75,000	84.9 (14.4)		
> $75,000 to $100,000	83.2 (16.4)		
> $100,000	84.9 (17.7)		
Insurance status (n = 144)			
Private insurance	83.1 (16.4)	0.32	0.8075
Medicare	80.4 (13.7)		
Medicaid	80.0 (20.0)		
Multiple	83.9 (15.1)		
Other	79.0 (0.00)		

Table 4.13 Relationships between Health-Related Quality of Life (Overall FACT-G Score) and Clinical/Demographic Variables Contd.

Marital status (n = 144)			
Single, in a relationship	80.7 (19.7)	0.36	0.8705
Single, not in a relationship	80.9 (11.7)		
Married	83.6 (16.8)		
Partner/Living together	85.1 (14.5)		
Divorced/Separated	79.3 (18.2)		
Widowed	85.7 (12.4)		
Stage of breast cancer at diagnosis (n = 144)			
Stage 0	77.3 (26.0)	0.41	0.8350
Stage 1	81.1 (14.1)		
Stage 2	84.6 (14.5)		
Stage 3	82.3 (16.7)		
Stage 4	84.0 (18.7)		
Do not know	77.8 (14.0)		
Time since breast cancer diagnosis (n = 145)			
1 year or less	80.5 (16.5)	1.34	0.2761
More than 1 year but less than 5 years	86.0 (14.9)		
More than 5 years but less than 10 years	85.6 (12.4)		
More than 10 years	81.1 (20.6)		

Pearson's correlation conducted for interval variables (age, number of comorbidities, number of treatment types received). ANOVA conducted for other variables.

The following multivariate study objectives and corresponding hypotheses were tested. The interaction term of cancer health literacy X patient activation was subsequently excluded since bivariate analysis did not show any significant relationship between the two constructs. Details of the hypotheses test results is described below. A summary is presented in Table 4.13.

4.6.1: To determine the overall predictive validity of the health literacy skills (HLS) framework in explaining cancer health-related quality of life using cancer health literacy and patient activation, controlling for clinical and demographic characteristics.

H4: Cancer health literacy and patient activation will explain a significant amount of variance in cancer health-related quality of life, controlling for clinical and demographic characteristics.

The hypothesis that cancer health literacy and patient activation would predict a significant amount of variance in cancer health-related quality of life was supported by the data ($F=10.31$; $df=4, 139$; $p<0.0001$). This supports the overall predictive validity of the health literacy skills (HLS) framework in explaining health-related quality of life. Twenty three percent of the variation in health-related quality of life ($R^2=0.23$) was accounted for by patient activation and two demographic/clinical characteristics (educational level and number of treatment types received), with an adjusted R^2 of 21 percent ($R^2= 0.21$). Therefore, hypothesis H4 was supported.

Hypotheses H5 and H6 could not be tested because there were very few reported incidents of cancer-related ED visits and hospitalizations. The overall predictive validity of the HLS framework in explaining the variance in these two dependent variables was not assessed.

4.6.2: To predict cancer health-related quality of life in breast cancer patients using cancer health literacy and patient activation controlling for clinical and demographic characteristics.

H7: Cancer health literacy and patient activation will be significant positive predictors of cancer health-related quality of life controlling for clinical and demographic variables.

Multiple linear regression analysis showed no significant relationship between cancer health literacy and health-related quality of life (B = -1.31, p = 0.77) while controlling for covariates (education and number of treatment types received). However, patient activation was positively related to health-related quality of life (B = 0.40, p < 0.0001) while controlling for education and number of treatment types received (Table 4.14). A 1-point increase in patient activation score was associated with a 0.4-point increase in health-related quality of life score. Therefore, hypothesis H7 was partially supported.

Hypotheses H8 and H9 could also not be tested because there were very few reported incidents of cancer-related ED visits and hospitalizations. The ability of cancer health literacy and patient activation to predict these two dependent variables was not assessed.

Table 4.14 Multiple Regression Analysis of Health Literacy Skills Framework (N=144)

Variables	**Unstandardized Coefficients**		**Standardized Coefficients**	**95% Confidence Intervals**		**p value**
	B	Std. Error	Beta	Lower bound	Upper bound	
Intercept	46.77	7.00		32.93	60.60	**<0.01**
Independent variables						
Cancer health literacy level	-1.31	4.47	-0.02	-10.14	7.52	0.77
Patient activation score	0.40	0.08	0.39	0.25	0.56	**<0.01**
Covariates						
Educational level	5.04	2.48	0.16	0.14	9.95	**0.04**
Number of treatment types received	2.75	1.12	0.18	0.53	4.97	**0.02**
F statistic=10.31; df=4, 139; Model p-value<0.0001; R^2=0.23; Adjusted R^2=0.21						

4.7 Summary of Study Findings

Four study objectives were not achieved. The two objectives to test the validity of the framework in explaining the variance in the number of cancer-related ED visits and cancer-related hospitalizations were not achieved because very few patients reported incidents of ED visits (3.4%, N=5) or hospitalizations (1.4%, N=2) resulting from their breast cancer in the last 30 days. In addition, the two objectives to predict these outcomes were not achieved. Table 4.15 contains details of the study objectives/hypotheses that were tested and corresponding results.

Table 4.15 Summary of Study Objectives and Hypotheses Test Results

Objectives/Hypotheses	Statistical Test	Results
Objective 1: To describe health literacy, patient activation, clinical (stage of breast cancer at diagnosis, time since diagnosis, type of breast cancer treatment received, comorbidities) and demographic (age, gender, educational level, ethnicity, household income, insurance status, marital status) characteristics of a breast cancer patient sample.	Mean, Standard deviation (SD), Frequency	• Average age 57.1 ± 10.8 years • 99% female • 53% had at least a college degree • 72% Caucasian • 66% had an annual household income over $50,000 • 60% had private insurance • 70% married or in a relationship • 92% had adequate cancer health literacy • 79% had adequate general health literacy • 68% in the higher levels (level 3 or 4) of activation • Equal distribution of patients from stage 1 to stage 4 • 78% had been diagnosed for the first time within the last 5 years • 79% had at least 1 comorbidity

Table 4.15 Summary of Study Objectives and Hypotheses Test Results Contd.

Objective 2: To examine the relationships between health literacy and clinical and demographic characteristics in a sample of breast cancer patients.	T test Fisher test	Cancer Health Literacy • Significant relationships with household income and educational level General Health Literacy • Significant relationships with age, educational level, and insurance
Objective 3: To examine the relationships between patient activation and clinical and demographic characteristics in a sample of breast cancer patients.	Correlation ANOVA	• Significant relationship with ethnicity
Objective 4: To assess the relationship between cancer health literacy and patient activation in a sample of breast cancer patients. **H1**: Breast cancer patients who have adequate cancer health literacy will have higher patient activation compared to those with limited cancer health literacy	T test	**Hypothesis H1 not supported**
Objective 5: To examine the relationship between cancer health literacy and patient-provider communication in a sample of breast cancer patients. **H2**: Breast cancer patients who have adequate cancer health literacy will have easier patient-provider communication and understanding of information provided compared to those that have limited cancer health literacy.	T test	**Hypothesis H2 not supported**
Objective 6: To examine the relationship between cancer health literacy and general health literacy in a sample of breast cancer patients. **H3**: There will be a significant positive relationship between cancer health literacy and general health literacy in the sample of breast cancer patients.	Chi-square test	**Hypothesis H3 supported**

Table 4.15 Summary of Study Objectives and Hypotheses Test Results Contd.

Objective 7: To determine the overall predictive validity of the health literacy skills (HLS) framework in explaining health outcomes (cancer health-related quality of life, cancer-related emergency department visits, and cancer-related hospitalizations), using cancer health literacy and patient activation, controlling for clinical/demographic characteristics. **H4**: Cancer health literacy and patient activation will explain a significant amount of variance in cancer health-related quality of life controlling for clinical and demographic characteristics. **H5:** Cancer health literacy and patient activation will explain a significant amount of variance in cancer-related emergency department visits controlling for clinical and demographic characteristics. **H6:** Cancer health literacy and patient activation will explain a significant amount of variance in cancer-related hospitalizations controlling for clinical and demographic characteristics.	Multiple linear regression: R^2; F test	**Hypothesis H4 supported** **Hypothesis H5 not tested** **Hypothesis H6 not tested**
Objective 8: To predict health-related quality of life in breast cancer patients using cancer health literacy and patient activation controlling for clinical and demographic characteristics. **H7**: Cancer health literacy and patient activation will be significant positive predictors of cancer health-related quality of life controlling for clinical and demographic variables.	Multiple linear regression: R^2; F test	**Hypothesis H7 partially supported**

Table 4.15 Summary of Study Objectives and Hypotheses Test Results Contd.

Objective 9: To predict cancer-related emergency department visits in breast cancer patients using cancer health literacy and patient activation controlling for clinical and demographic characteristics. **H8**: Cancer health literacy and patient activation will be significant negative predictors of cancer-related emergency department visits controlling for clinical and demographic characteristics.	Multiple linear regression: R^2; F test	**Hypothesis H8 not tested**
Objective 10: To predict cancer-related hospitalizations in breast cancer patients using cancer health literacy and patient activation controlling for clinical and demographic characteristics. **H9**: Cancer health literacy and patient activation will be significant negative predictors of cancer-related hospitalizations controlling for clinical and demographic characteristics.	Multiple linear regression: R^2; F test	**Hypothesis H9 not tested**

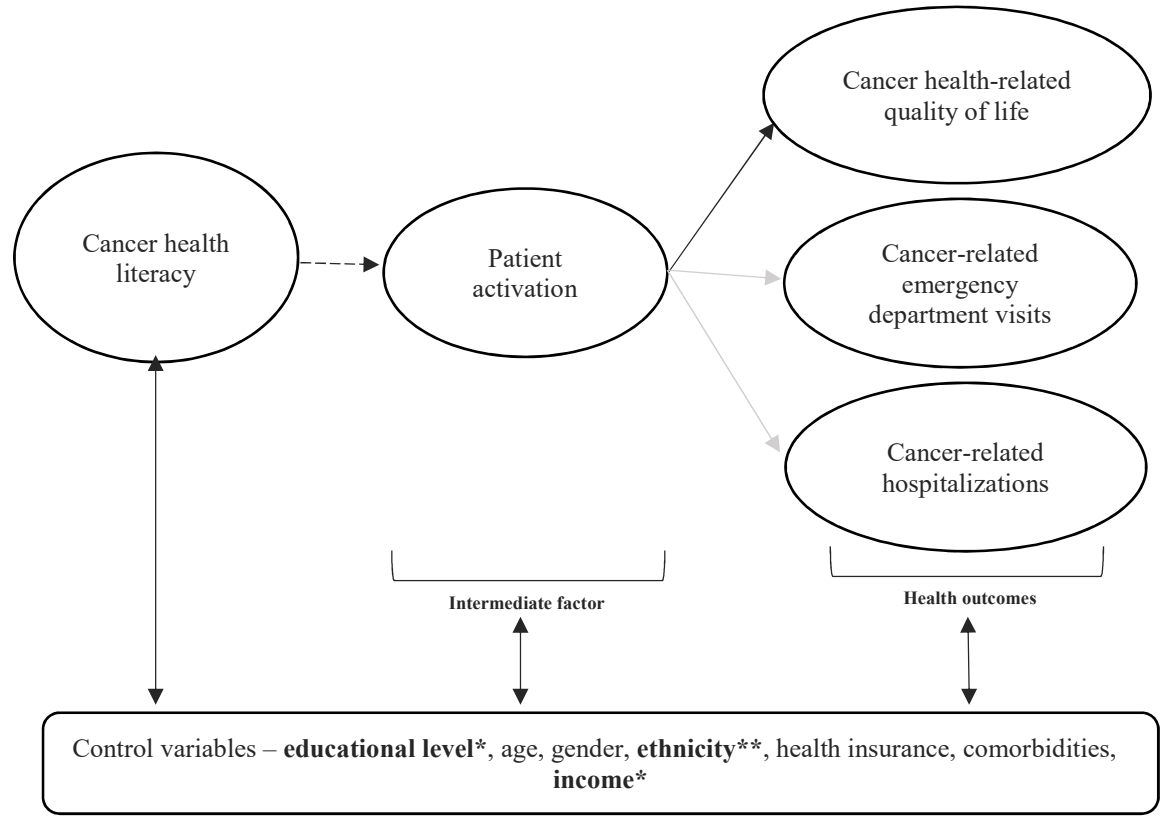


Figure 4.2 Health Literacy Skills Framework Showing Significant Relationships

Chapter 5: Discussion and Conclusion

This study assessed health literacy and patient activation in HER-2 positive breast cancer patients and also examined the ability of these constructs to explain and predict health outcomes using the Health Literacy Skills (HLS) framework. This study also explored the relationships of health literacy and patient activation with clinical/demographic patient characteristics. In addition, the relationship of general health literacy and patient activation with cancer health literacy was examined. Lastly, the relationship between cancer health literacy and patient-provider communication was assessed.

This chapter consists of five sections. The first section contains a discussion of study findings and possible explanations of the findings. The second section explores the implications of study findings. The third section discusses the study limitations, and the last two sections consist of suggestions for future research and the conclusion.

5.1 Discussion of Study Findings

5.1.1 Participation Rate and Study Sample Characteristics

The participation rate of this study was high as almost 90 percent (N=146) of patients who were approached by clinic staff and offered participation in the study, gave their consent to participate and completed the survey. This high participation rate could have resulted because the approached patients were interested in contributing to the potential improvement of breast cancer care experience and also because they were asked to complete the survey during their office visit.

The average age of study participants was 57.1±10.8 years which coincides with the average age at breast cancer diagnosis of 61 years in United States women. About 19

percent of breast cancer cases occur among women younger than 50 years, while 44 percent occur in women older than 65 years.[2] Since breast cancer affects many more women than men,[56] it was not surprising that 99 percent of study participants were female. Only one male participated in the study. The study participants were predominantly Caucasian (71.7%), married or in a relationship (69.5%), had a high formal education level (52.8%), had private insurance (59.7%), and had an annual household income over $50,000 (66.2%). These characteristics suggest that this sample of breast cancer patients were socioeconomically advantaged.

Clinically, the study participants were almost equally distributed from cancer stage 1 to stage 4 with about half being newly diagnosed (within the last year) breast cancer patients (N=73). Also, a majority of the patients (73.3%) had at least one comorbidity. This was not surprising, given the average age of study participants, as the prevalence of comorbidity increases with age. A study published by Fu et al. in 2015 which evaluated the association of comorbidities with quality of life in breast cancer survivors showed that 73.8 percent of the 134 breast cancer survivors had at least one comorbidity.[150]

Even though the majority of breast cancer patients in this study were Caucasian, the United States breast cancer population is more varied, with Blacks being almost as much as Caucasians, and Hispanics being slightly less than Asian/Pacific Islanders. However, there is a disproportionate death rate resulting from breast cancer among Black breast cancer patients with about eight more deaths per 100,000 occurring in black women than in white women. Black breast cancer patients also have a five-year relative survival rate that is 10 percent lower than that of white women.[151] These disparities have been attributed to socioeconomic disadvantages as well as differences in the clinical manifestation of breast cancer in this sub-population. Black breast cancer patients are more likely to be diagnosed at a later stage and have an aggressive type of breast cancer (triple

negative). They are also more likely to have insurance-related barriers to accessing health care.[152-154] In Hispanics, the lower rate of breast cancer incidence and mortality compared to non-Hispanic Whites might not necessarily be a true picture of reality. These lower rates could partially be attributed to lower rates of mammography utilization and delayed follow-up of abnormal screening results in this sub-population.[155,156] It is therefore important for healthcare providers to be mindful of the barriers that might affect ethnic minorities in having optimal breast cancer outcomes and be proactive in helping such patients overcome avoidable barriers.

5.1.2 Primary Study Variables

Health Literacy in Breast Cancer Patients

The majority of participants had adequate cancer health literacy (92%, N=134) and adequate general health literacy (79%, N= 114) based on their CHLT-6 and NVS scores, respectively. Even though these two constructs had a significant relationship with each other, the higher percentage of patients with adequate cancer health literacy confirms that the cancer health literacy tool has more specificity in assessing the health literacy level of cancer patients. There were also significant relationships between cancer health literacy and household income and educational level. Patients with higher incomes and formal education showed adequate cancer health literacy compared to their counterparts. General health literacy was also related to higher formal education, younger age and having private insurance.

These sociodemographic differences in health literacy (cancer-specific and general) corroborate extant literature in both cancer and non-cancer populations which support a positive relationship between health literacy and socioeconomic status. For example, Dumenci et al. described the development of the 30-item and 6-item cancer health literacy

instruments designed to measure cancer health literacy along a continuum and identify patients with limited cancer health literacy, respectively. The study population consisted of a wide variety of cancer patients including breast, colon, gastrointestinal, skin, and hematologic cancers. Results showed that compared to individuals with adequate cancer health literacy (CHL), those with limited CHL were likely to be Black, have a low educational level, have a low income, not be privately insured, and most likely did not engage in health decisions.[18]

In another study, Rikard et al. found that health literacy had a significantly negative association with age, but a significantly positive association with household income and education in a population of 14,592 United States adults who took the 2003 National Assessment of Adult Literacy (NAAL). Health literacy level increased by a quarter of a point for every additional thousand dollars in median household income, while it increased by nearly four points for each additional level of educational attainment.[157]

Patient Activation in Breast Cancer Patients

Patient activation, a secondary independent variable, was relatively high (65.9±15.7), resulting in the majority of breast cancer patients (68%, N= 99) being in the higher activation levels (PAM level 3 or 4). Patient activation was significantly higher in Caucasians (68.9±16.0) compared to Blacks (54.5±6.9) and Hispanics (58.3±10.7).

This result is similar to findings of other studies which showed that ethnic minorities including Blacks and Hispanics are more likely to have lower patient activation than Caucasians. Hibbard et al.'s 2008 study that explored the role that patient activation may have in racial and ethnic health disparities revealed that mean patient activation score for Caucasians was four points higher than that of African Americans in both national and Medicaid samples.[158] Using the 2007 Health Tracking Household Survey, Cunningham et

al. found similar patterns whereby compared to Caucasians and African Americans, Hispanics had much lower levels of patient activation with only 24.8 percent of Hispanics at the highest level of patient activation (PAM level 4), compared to 39.5 percent of Blacks and 45.3 percent of Whites.[35,36]

Patients with low activation levels are more likely to have unmet medical needs and delay medical care, compared with more activated patients.[29] In addition, they are less likely to be aware of treatment guidelines for their condition or seek out health information.[30] These behavior patterns foster avoidable misuse of scarce healthcare resources including a greater number of visits to the emergency department and hospitalizations.[159,160] Low patient activation in breast cancer patients could result in patients being less capable of accessing available medical resources for managing breast cancer. Such patients might also find it more difficult to coordinate care among different providers, and not readily identify symptoms that signify worsening of health or a relapse/recurrence.

Consequently, it is important for health care providers to understand that a patient's ability to manage their health and healthcare are inextricably tied to their social and economic circumstances. These social determinants are related to patient activation and should inform interactions to meet patients at their level. Adopting a one-size-fits-all approach for encouraging breast cancer patients to proactively manage their care will most likely miss the mark for a significant number of breast cancer patients.

Cancer Health Literacy and Patient Activation

Health literacy is related to the ability to use information in making health-relevant decisions while patient activation is associated with chronic disease self-management.[47] Studies that have investigated the relationship between health literacy and patient activation show conflicting results – some have found a weak positive correlation while others have found no association between the two constructs. A study by Smith et al. showed a weak, positive correlation between general health literacy and patient activation ($r=0.11$, $p=0.005$) among an older (aged 55 to 74 years) sample of patients who received care from a primary care clinic or one of three federally qualified health centers in Chicago, Illinois. In their study, 31.3 percent of study participants had limited literacy skills according to the Test of Functional Health Literacy in Adults (TOFHLA), while 83.5 percent were in the highest category of patient activation (PAM level 4).[44] Another study by Dunlay et al. also showed a positive association between health literacy and patient activation in a sample of 302 elderly patients who were hospitalized with acute decompensated heart failure at Mayo Clinic hospitals in Rochester, Minnesota. Health literacy was assessed using a 3-item Health Literacy Screener, and 28 percent of patients had poor health literacy according to this measure. These patients with poor health literacy had low patient activation as well.[161]

Conversely, Couture et al. found no association between general health literacy and patient activation (biserial correlation – rb: 0.075, $p = 0.07$) among patients with chronic diseases including diabetes, cardiovascular disease, respiratory disease, musculoskeletal disease, and chronic pain. Most study participants had considerable illness burden, with an average of six chronic diseases. 67.5 percent of patients had limited health literacy as measured by the Newest Vital Sign (NVS), while 65.1 were in the higher levels of activation (PAM levels 3 and 4).[162]

The relationship between cancer health literacy and patient activation was not significant in this population of breast cancer patients, even though a positive and significant relationship was expected. This might have been because a majority of study participants had adequate cancer health literacy as measured by the CHLT-6. The limited variability in cancer health literacy level of study participants could have contributed to the non-significance of study results.

Cancer Health Literacy and Patient-Provider Communication

The majority of patients found it easy both to communicate their breast cancer concerns to their healthcare provider and to understand information given by healthcare providers about breast cancer and its management. However, there was no significant difference in the ease of communicating breast cancer concerns to a healthcare provider between patients with limited cancer health literacy (4.5±0.7) and patients with adequate cancer health literacy (4.6±0.7). Also, there was no significant difference in the ease of understanding information given by healthcare providers about breast cancer and its management between patients with limited cancer health literacy (3.7±1.2) and patients with adequate cancer health literacy (4.3±0.8).

The relationship between health literacy and patient-provider communication might not have been significant due to a ceiling effect as most patients found it easy to communicate with their providers and understand information. However, a cancer patient's health literacy level plays an important role in his or her ability to discuss disease, treatment options, and prognosis with a healthcare provider in a meaningful way. In a study by Williams et al. that aimed to explore and identify communication and decision making between health care providers and African American cancer patients/caregivers, participants consistently described the importance of communication with their physicians

to overall quality of life. They also stressed the importance of the physician connecting with patients (and their families) on a personal level as this would foster conversations where the information provided is appropriate for patients' health literacy level as well as their stage of acceptance/denial of the disease and care options.[163]

The National Cancer Institute and the Institutes of Medicine have emphasized that high quality cancer care involves patient-centered communication with healthcare providers.[164-166] When healthcare providers effectively communicate with cancer patients and their families, there are improvements in patients' quality of life, satisfaction with care, and health outcomes.[167] It is thus important for healthcare providers to ensure that communication with cancer patients encompasses follow-up care, side effects of cancer treatment, emotional/social cancer-related needs, and lifestyle recommendations.[168,169] Since it might be overwhelming to effectively discuss issues in these four areas in one visit, interactions could be designed to provide information relevant to individual patient's literacy level and position in the cancer care journey. Also, keeping tabs on areas that have been discussed in patient records could enable healthcare providers to easily identify areas that have not been covered and subsequently ensure that they are addressed with the patient in future clinic visits. Healthcare providers could further optimize interactions with patients by using plain language as much as possible, using pictures to support spoken directions, presenting recommendations as action plans, and soliciting patient feedback to ensure comprehension.[21,170,171]

5.1.3 Evaluation of Health Literacy Skills (HLS) Framework

The HLS framework describes how health literacy affects health outcomes such as health status, emergency care, and hospitalization through intermediate factors including disease and self-care knowledge.[123] The patient activation measure was used to assess

disease and self-care knowledge, while the CHLT-6 measured cancer health literacy. The only health outcome measure evaluated in this study was health status (cancer health related quality of life) because there were too few reported incidents of cancer-related ED visits and hospitalizations.

Study findings supported the overall predictive validity of the HLS framework in explaining health-related quality of life ($F=10.31$; $df=4, 139$; $p<0.0001$), in that twenty three percent of the variation in cancer health-related quality of life could be explained by cancer health literacy, patient activation, educational level, and number of treatment types received. Higher patient activation was related to higher health-related quality of life even after accounting for cancer health literacy, education and number of treatment types received. A 1-point increase in patient activation score was associated with a 0.4-point increase in overall quality of life score, holding other predictors in the model constant. Cancer health literacy was not predictive.

Our findings are supported by other studies that have investigated the relationship between patient activation and quality of life. Magnezi et al. reported a significant positive correlation between patient activation and the total quality of life scores as measured by Short Form-12 Health Survey (SF-12), as well as the physical and mental health subscale scores in primary care patients. Participants generally had a high quality of life (32.1 ± 8.3, range of 12 to 44).[172]

Another study by Blakemore et al., showed that patient activation was significantly lower in individuals with poor health literacy and higher in those with good quality of life in a large cohort of older adults (65 years and older). The Single Item Literacy Screener (SILS) was used to measure health literacy and the EuroQol EQ-5D-5L health utility index was used to measure health related quality of life.[173] These results support the association between quality of life and patient activation. The non-significance of the relationship

between health literacy and patient activation in this study may be due to the dichotomous nature of the cancer health literacy instrument used.

5.2 Summary and Implications

Study participants were found to have high levels of health literacy and patient activation in general. This was not surprising as most of the breast cancer patients were socioeconomically advantaged, and socioeconomic status is positively associated with these constructs.[90,133] The cancer health literacy instrument (CHLT-6) also showed more specificity in detecting breast cancer patients' health literacy level compared to the general health literacy instrument (NVS). With regards to patient-provider interaction, study participants mostly found it easy to communicate their breast cancer concerns to their healthcare provider and also understand information given by healthcare providers about breast cancer and its management.

Study participants generally reported a high health-related quality of life. However, only a few patients reported cancer-related ED visits and hospitalizations, so the relationship of resource utilization with health literacy and patient activation could not be assessed. Finally, the HLS framework was significant, with cancer health literacy, patient activation, educational level, and number of treatment types received explaining over a fifth of the variance in patients' health-related quality of life.

Breast cancer is no longer viewed as a terminal disease but is now considered to be a chronic condition due to improvements in detection, diagnosis, and treatment.[174] Increasingly, patients with chronic diseases, including breast cancer, are being expected to participate in managing their care. This study's findings further validate extant literature that patients' involvement in self-managing their health and healthcare (patient activation) is positively associated with quality of life.[133,172,173] To our knowledge, this is the first study

to specifically explore this relationship in breast cancer patients. In addition to improved quality of life, higher patient activation levels have been associated with better health outcomes and resource utilization in other chronic conditions including diabetes, heart failure, and asthma.[38,160] It is not far-fetched to assume that such associations would also apply in breast cancer patients.

Highly activated cancer patients tend to be better informed and more proactive about managing their condition.[37] They are also more likely to understand their diagnosis, efficiently manage side effects, feel sufficiently informed about their treatment plan, and have their values reflected in their treatment plans. Furthermore, poorly activated cancer patients tend to be less satisfied with their care.[122] Therefore, cancer care providers should consider assessing patient activation at the beginning of cancer care and subsequently encouraging their breast cancer patients to participate in managing their care as a quality metric of care. The patient-provider discourse about self-management in the oncology space can also be designed to accommodate all patients irrespective of their health literacy level, and could encompass issues relevant to the cancer patient including support of patient autonomy, guidance to navigate the healthcare system, and access to resources.[166]

5.3 Study Limitations

This study was adequately powered, and patients were recruited from multiple clinics in Texas. However, there are some study limitations that should be considered while interpreting study findings. These are discussed in detail below.

First, all the data used in the study were self-reported. There was no objective validation of participants' responses which could have been subject to recall bias or a desire to please. Another limitation to this study is selection bias as a result of convenience sampling. Patients who participated in this study volunteered to do so. It is possible that

patients with high health literacy and high patient activation levels were more likely to be interested in being part of a study that could potentially improve breast cancer patients' care experience. Also, clinic staff might have been more likely to offer such patients participation in the study. Next, given the descriptive and cross-sectional nature of this study, causality cannot be inferred. Even though the study sample was from multiple clinics within a Texas-based oncology group, the findings might still not be representative of the breast cancer population in Texas or nationally, particularly because most of the study participants were socioeconomically advantaged. In addition, the participating oncology clinics implement the Oncology Care Model (OCM) and other value-based care models designed to improve patient care and the cancer treatment experience. Consequently, the study results can only be generalizable to breast cancer patients similar to those that participated in the study and receive care from similar types of practices. In addition, the recall period (30 days) for the items measuring the number of cancer-related ED visits and hospitalizations in this sample of breast cancer patients might have been too short to adequately capture these outcome measures. Finally, the patient activation score of study participants pertained to their knowledge/ability to self-manage their breast cancer care and may not necessarily indicate how they would manage other comorbidities/chronic conditions.

5.4 Suggestions for Future Research

Future research could further validate the HLS framework by exploring the relationship of health outcomes such as the number of cancer-related ED visits and hospitalizations with health literacy and patient activation using a longer recall period. This might yield actual results even though the chances of recall bias would be higher.

Alternatively, the number of ED visits and hospitalizations could be objectively obtained from electronic medical records or a healthcare database, if available.

In addition, other studies that explore cancer health literacy might yield significant findings with a non-dichotomous cancer health literacy instrument like the CHLT-30. Even though the CHLT-6 adequately distinguishes individuals with limited health literacy from those with adequate health literacy, it does not detect degrees of limitedness or adequacy of cancer health literacy. Therefore, it might be more useful in future studies to use the longer 30-item cancer health literacy tool, or a similar instrument, which measures cancer health literacy along a continuum.

5.5 Conclusion

This study lends support to the utility of the HLS framework in predicting health-related quality of life in HER-2 positive breast cancer patients. Findings show that both modifiable factors such as patient activation and number of treatment types as well as a non-modifiable factor (education) were significant and positive predictors of quality of life. In addition, Blacks and Hispanics were found to have significantly lower patient activation levels than Caucasians. Paying attention to these factors in interventions aimed to improve quality of life are recommended. Cancer health literacy was not predictive, although the high levels and homogeneity of cancer health literacy among study participants could have impacted the results. Further assessments of health literacy and patient activation with quality of life as well as other health outcomes in larger and more diverse populations of breast cancer patients are warranted.

Appendices

Appendix 1: Survey Instrument

Patient study number: _____

Section 1: We would like to better understand your needs for information about breast cancer. This set of questions involves basic cancer health information. Please check the option that best corresponds to your answer for each question.
1. The normal range for hemoglobin for a male is 13.3 to 17.2g/dl. Joe's hemoglobin is 9.7g/dl. Is Joe within the normal range? □ Yes □ No
2. A biopsy of a tumor is done to _____ □ Remove it □ Diagnose it □ Treat it
3. If a patient has stage 1 cancer, it means the cancer is _____ □ Localized □ In nearby organs □ In distant sites
4. The role of a physical therapist is to talk to a patient about emotional needs. □ True □ False
5. A tumor is considered ''inoperable'' when it cannot be treated with _____ □ Radiation therapy □ Surgery □ Chemotherapy
6. Sally will get radiation therapy once a day, Monday through Friday. If Sally has therapy for 4 weeks, how many times will she get radiation therapy? □ 5 □ 15 □ 20

Appendix 1: Survey Instrument Contd.

Section 2: We would also like to understand your ability to interpret general health information. This set of questions require you to find and interpret information presented on a nutrition label for a pint of ice cream. Please fill in your response for each question.

Nutrition Facts	
Serving Size	½ cup
Servings per container	4
Amount per serving Calories 250	Fat Cal 120
	%DV
Total Fat 13g	20%
Sat Fat 9g	40%
Cholesterol 28mg	12%
Sodium 55mg	2%
Total Carbohydrate 30g	12%
Dietary Fiber 2g	
Sugars 23g	
Protein 4g	8%

*Percentage Daily Values (DV) are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs

Ingredients: Cream, Skim Milk, Liquid Sugar, Water, Egg Yolks, Brown Sugar, Milkfat, Peanut Oil, Sugar, Butter, Salt, Carrageenan, Vanilla Extract.

7. If you eat the entire container, how many calories will you eat? _____

8. If you are allowed to eat 60g of carbohydrate as a snack. How much ice-cream could you have? _____

9. Your doctor advises you to reduce the amount of saturated fat in your diet. You usually have 42g of saturated fat in your diet each day which includes 1 serving of ice cream. If you stopped eating ice cream, how many grams of saturated fat will you be consuming daily? _____

10. If you usually eat 2500 calories in a day, what percentage of your daily value of calories will you be eating if you eat one serving? _____

Pretend that you are allergic to the following substances: Penicillin, peanuts, latex gloves, and bee stings

11. Is it safe for you to eat this ice cream? ____

12. If no, why not? _____

Appendix 1: Survey Instrument Contd.

Section 3: This set of questions asks about your involvement in managing your breast cancer. Please check the option that best corresponds to your response for each question.					
	Disagree Strongly	**Disagree**	**Agree**	**Agree Strongly**	**N/A**
13. When all is said and done, I am the person who is responsible for managing my breast cancer.	□	□	□	□	□
14. Taking an active role in my own breast cancer care is the most important factor in determining my health and ability to function.	□	□	□	□	□
15. I am confident that I can take actions that will help prevent or minimize some symptoms or problems associated with my breast cancer.	□	□	□	□	□
16. I know what each of my prescribed breast cancer medications does.	□	□	□	□	□
17. I am confident that I can tell when I need to go get medical care and when I can handle a breast cancer-related problem myself.	□	□	□	□	□
18. I am confident I can tell a doctor breast cancer-related concerns I have even when he or she does not ask.	□	□	□	□	□
19. I am confident that I can follow through on breast cancer medical treatments I need to do at home.	□	□	□	□	□
20. I understand the nature and causes of my breast cancer.	□	□	□	□	□
21. I know the different medical treatment options available for my breast cancer.	□	□	□	□	□
22. I have been able to maintain the lifestyle changes for my health that I have made.	□	□	□	□	□
23. I know how to prevent further problems with my health.	□	□	□	□	□

Appendix 1: Survey Instrument Contd.

	Disagree Strongly	Disagree	Agree	Agree Strongly	N/A
24. I am confident I can figure out solutions when new situations or problems arise with my health.	□	□	□	□	□
25. I am confident I can maintain lifestyle changes, like diet and exercise, even during times of stress.	□	□	□	□	□

Section 4: Below is a list of statements that other people with breast cancer have said are important. Please select one number per line to indicate your response as it applies to the past 7 days.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
Physical well-being					
26. I have a lack of energy.	0	1	2	3	4
27. I have nausea.	0	1	2	3	4
28. Because of my breast cancer, I have trouble meeting the needs of my family.	0	1	2	3	4
29. I have pain.	0	1	2	3	4
30. I am bothered by side effects of breast cancer treatment.	0	1	2	3	4
31. I feel ill.	0	1	2	3	4
32. I am forced to spend time in bed.	0	1	2	3	4
Social/family well-being					
33. I feel close to my friends.	0	1	2	3	4
34. I get emotional support from my family.	0	1	2	3	4
35. I get support from my friends.	0	1	2	3	4
36. My family has accepted my breast cancer.	0	1	2	3	4
37. I am satisfied with family communication about my breast cancer.	0	1	2	3	4
38. I feel close to my partner (or the person who is my main support).	0	1	2	3	4

Appendix 1: Survey Instrument Contd.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box ☐ *and go to the next question.* 39. I am satisfied with my sex life.	0	1	2	3	4
Emotional well-being					
40. I feel sad.	0	1	2	3	4
41. I am satisfied with how I am coping with my breast cancer.	0	1	2	3	4
42. I am losing hope in the fight against my breast cancer.	0	1	2	3	4
43. I feel nervous.	0	1	2	3	4
44. I worry about dying.	0	1	2	3	4
45. I worry that my breast cancer will get worse.	0	1	2	3	4
Functional well-being					
46. I am able to work (include work at home).	0	1	2	3	4
47. My work (include work at home) is fulfilling.	0	1	2	3	4
48. I am able to enjoy life.	0	1	2	3	4
49. I have accepted my breast cancer.	0	1	2	3	4
50. I am sleeping well.	0	1	2	3	4
51. I am enjoying the things I usually do for fun.	0	1	2	3	4
52. I am content with the quality of my life right now.	0	1	2	3	4
Section 5: The next 2 questions are about how often (if at all) severe breast cancer symptoms have resulted in you visiting the emergency department or being hospitalized. Please fill in the blank space for each question.					
53. Within the last one month, how many emergency department visits have you had due to a breast cancer complication? _____ (indicate the number of times)					
54. Within the last one month, how many hospitalizations have you had due to a breast cancer complication? _____ (indicate the number of times)					

Appendix 1: Survey Instrument Contd.

Section 6: The next 2 questions are about how you communicate with your health provider(s) about breast cancer. Select the option that best corresponds to your answer for each question.

55. How difficult is it for you to communicate your concerns about your breast cancer to your healthcare provider(s)?
□ Extremely difficult
□ Somewhat difficult
□ Neither easy nor difficult
□ Somewhat easy
□ Extremely easy

56. How difficult is it for you to understand the information provided by your healthcare provider(s) about your breast cancer and its management?
□ Extremely difficult
□ Somewhat difficult
□ Neither easy nor difficult
□ Somewhat easy
□ Extremely easy

Section 7: Finally, we would like to learn a little about you and the present state of your breast cancer. Please fill in your response or select the option that best corresponds to your answer for each question.

57. What year were you born in? _____

58. Which option best describes your gender?
□ Male
□ Female
□ Transgender
□ Other

59. Which of the following best describes your race/ethnicity?
□ African-American or non-Hispanic black
□ American Indian or Alaska Native
□ Asian-American or Pacific Islander
□ Caucasian or non-Hispanic white
□ Mexican-American or Hispanic
□ Other (please specify) _____

60. What is your highest level of education?
□ Less than High School
□ High School Graduate or GED
□ College graduate
□ Postgraduate (e.g., MD, MS, PhD)
□ Other (*please specify*) _____

Appendix 1: Survey Instrument Contd.

61. Which option best describes your annual household income?
□ Less than $25,000
□ $25,000 to $50,000
□ > $50,000 to $75,000
□ > $75,000 to $100,000
□ >$100,000

62. Which option best describes the type of health insurance you currently have?
□ No insurance/Self-pay
□ Private insurance (e.g. BlueCross/Blue Shield, Humana)
□ Medicare
□ Medicaid
□ Not sure
□ Other (*please specify*) _____

63. Which option best describes your marital status?
□ Single, in a relationship
□ Single, not in a relationship
□ Married
□ Partner/Living together
□ Divorced/Separated
□ Widowed

64. At what stage was your breast cancer diagnosed?
□ Stage 0
□ Stage 1
□ Stage 2
□ Stage 3
□ Stage 4
□ Do not know

65. How long ago were you first diagnosed with breast cancer?
□ 1 year or less
□ More than 1 year but less than 5 years
□ More than 5 years but less than 10 years
□ More than 10 years

66. Besides chemotherapy, what other type of breast cancer treatment have you received? *Check all that apply*.
□ Radiation therapy
□ Surgery (e.g. lumpectomy, mastectomy)
□ Hormone therapy (e.g. Tamoxifen, Arimidex, Fareston, Femara, Falsodex, Aromasin)
□ Other (*please specify*) _____

67. In addition to breast cancer, what other illnesses do you have? *Check all that apply*.

□ Asthma □ Arthritis □ Diabetes □ Hypertension
□ High cholesterol □ Heart disease □ Anxiety □ Depression
□ Thyroid problems □ Kidney problems □ Other (*please specify*) _____

This is the end of the survey. Thank you for participating!

Appendix 2: Cover Letter

COLLEGE OF PHARMACY
THE UNIVERSITY OF TEXAS AT AUSTIN

Health Outcomes and Pharmacy Practice Division • 1 University Station A1930 • Austin, TX 78712-0127
Phone: (512) 471-6892 • FAX (512) 471-8762

Dear Patient,

You are invited to participate in a study titled "**Relationship between Health Literacy, Patient Activation, and Health Outcomes in Breast Cancer Patients.**" The study is being conducted by Chisom Kanu, M.Pharm, for her dissertation project along with Carolyn Brown, PhD, College of Pharmacy of The University of Texas at Austin, and Dr. Lalan Wilfong Texas Oncology, Austin, Texas. Kindly read the information below carefully before deciding whether or not to take part. Completing the survey will be taken as evidence of your consent to participate in the study.

The purpose of this research study is to assess your understanding of basic cancer information, your ability to manage your health, as well as how this understanding of cancer information and self-management abilities affect your health. You will be required to complete one survey during this clinic visit which should take no more than 10 minutes to complete. The study will include approximately 150 breast cancer patients.

Your participation in the study will help facilitate the provision of appropriate information to breast cancer patients thereby increasing patient ability to be involved in self-managing their health and having better outcomes.

If you agree to participate:

- The survey will take approximately 10 minutes of your time.

Benefits/Risks/Confidentiality of Data

There are no direct benefits from participating in this study. However, the findings of this study could help to increase the effectiveness of interventions to improve breast cancer patients' involvement in managing their health. Also, the risk of participating in this study is considered minimal by the University of Texas at Austin Institutional Review Board. Your privacy and confidentiality will be protected by having clinic staff assign unique numbers to each study participant. Consequently, no individual response will be linked back to you. In addition, all completed surveys will be permanently deleted upon completion of the study and acceptance of manuscript(s).

If it becomes necessary for the Institutional Review Board to review the study records, information that can be linked to you will be protected to the extent permitted by law. Your research records will not be released without your consent unless required by law or a court order.

Participation or Withdrawal

Your participation in this study is voluntary and free of charge. You may decline to answer any question and you have the right to withdraw from participation at any time. Withdrawal will not affect your medical care, or your relationship with The University of Texas at Austin in any way. If you do not want to participate, simply stop answering the survey questions. You will be given the survey to complete by clinic staff at this clinic appointment.

Contact information

Prior, during, or after your participation in this study, you can contact Chisom Kanu at 469-353-0844 or send an email to ckanu@utexas.edu if you encounter any problems or have any questions regarding the study.

Questions about your rights as a research participant

If you have questions about your rights or are dissatisfied at any time with any part of this study, you can contact, anonymously if you wish, the University of Texas at Austin Institutional Review Board by phone at (512) 471-8871 or email at orsc@uts.cc.utexas.edu.

Thank you for your participation.

Appendix 3: Study Site Letter of Support

TEXAS ONCOLOGY

Study Site Letter of Support

February 27th, 2018

Carolyn M Brown, PhD
The University of Texas at Austin
College of Pharmacy
Health Outcomes and Pharmacy Practice division
1 University Station A1930
Austin, TX 78712-0120

Dear Dr. Brown:

I am pleased to provide support for the proposed study titled: "Relationship between Health Literacy, Patient Activation, and Health Outcomes in Breast Cancer Patients" which will be conducted in our clinic. Here at Texas Oncology, we are constantly looking for innovative ways to provide the best medical care for our patients with breast cancer. Consequently, we are pleased to confirm that we will partner with you to ensure the successful execution of the proposed project.

We will work with your team, including Chisom Kanu, and have our clinic research staff identify and obtain consent from eligible patients to be included in the study. We will also assist you with data collection by giving out the surveys to patients who give their consent to participate in the study during clinic visits. I have participated in the development of the proposed study protocol and I will ensure that the research protocol is followed in conducting the study. In addition, I will contribute to planning the dissemination of study findings. My contribution to this study is free of charge because it is an unfunded study.

Sincerely,

Lalah Wilfong, M.D.

Appendix 4: Informed Consent Tracking Log

STUDY TITLE: The Relationship between Health Literacy, Patient Activation, and Health Outcomes in Breast Cancer Patients		
PROTOCOL NO.: T0-1821	**TEXAS ONCOLOGY CO-INVESTIGATOR:** Lalan S. Wilfong, MD	**SITE NAME:**

Date	**Patient Study ID Number**	**Informed Consent Given? Y/N**

Appendix 5: Survey Evaluation Form

Please evaluate the survey you just completed based on your experience with breast cancer and the care process. Kindly respond to the following questions as best as you can. Check Yes or No and add comments as appropriate.

Readability of questions

	Yes	**No**
Were all the questions **clear**?		
Were all the questions **easy to understand**?		

If you answered no, please specify which question(s) was problematic:

Relevance of questions

	Yes	**No**
Were all the questions **relevant to the research topic**?		
Were there any **missing issues of importance**?		

Please provide more details below:

Format of survey

	Yes	**No**
Was the survey layout **user friendly**?		
Did you find it **hard to follow**?		

Kindly state any suggestions for improvement below:

Time to complete the survey

	Yes	**No**
Did the survey take **more than 10 minutes to complete**?		

If you answered yes, please specify how long it took you to complete (in minutes):

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